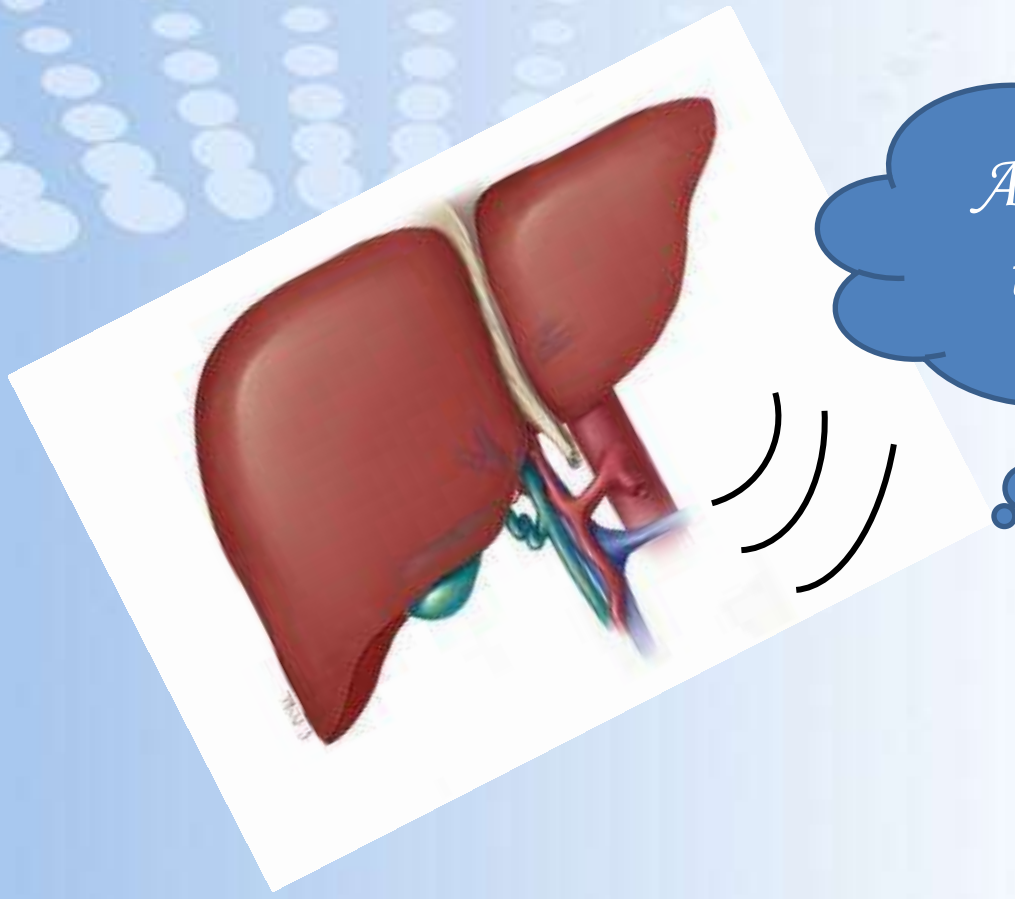
AKI in Hepatic Patients

By

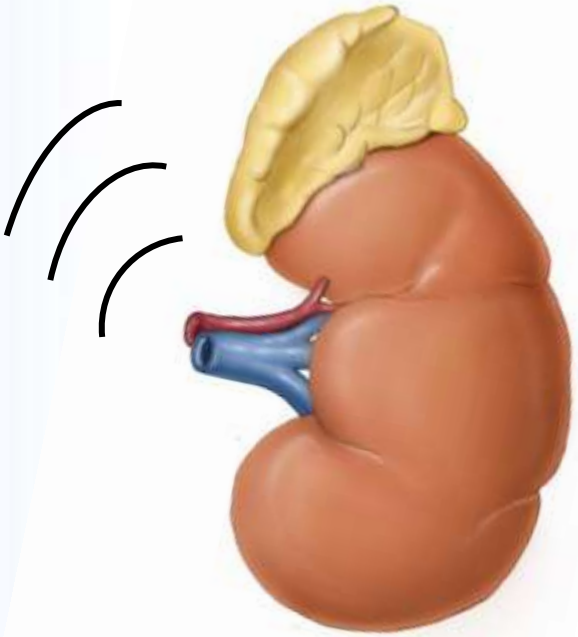
Hanaa Okda

Lecturer of Internal Medicine &Nephrology
Tanta university

Question ?

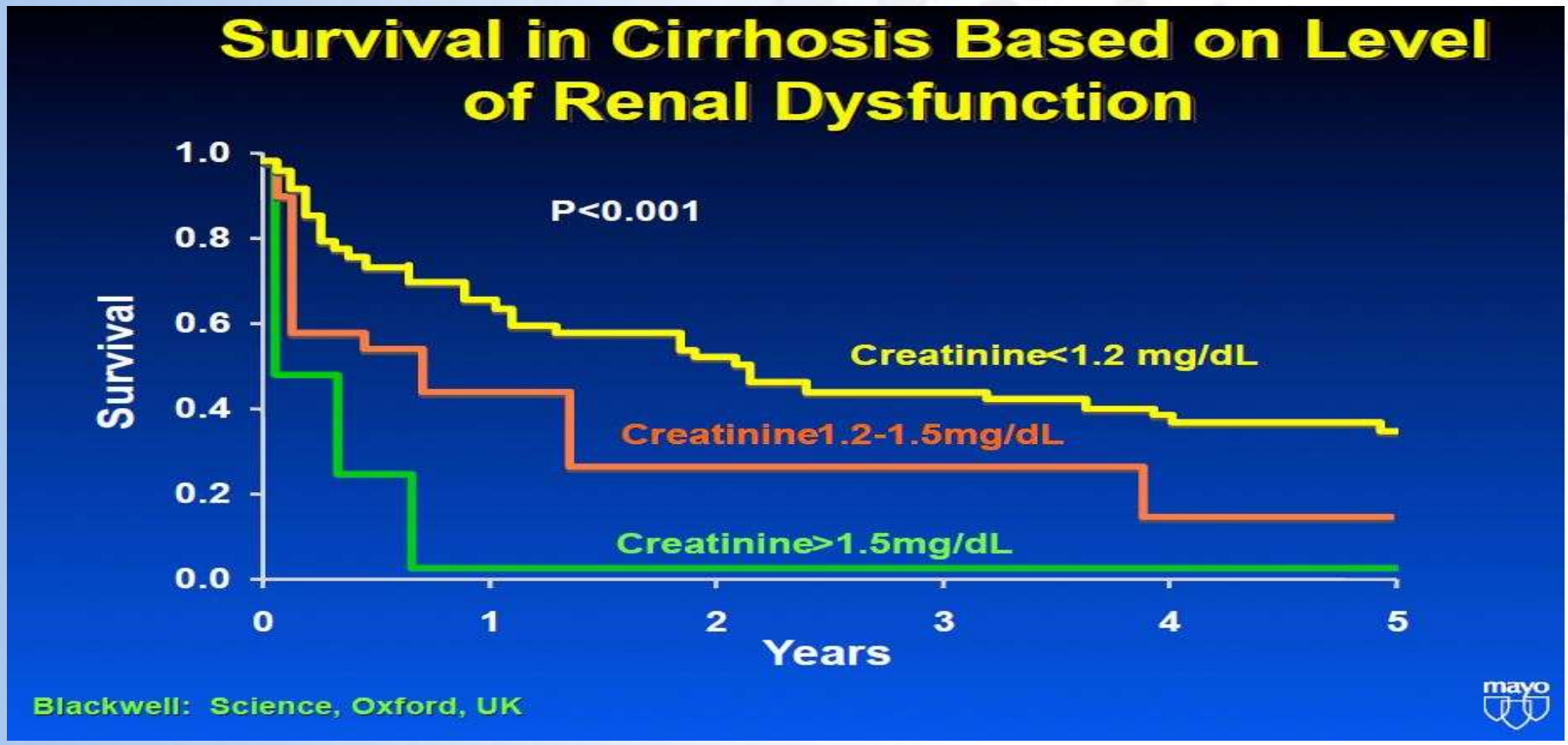


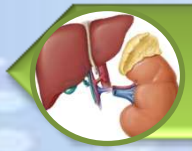
Are they talking to each other?



Are they talking to each other?

- Parameters of renal functions were found to be a powerful predictor of death in decompensated cirrhosis. Higher SCr consistently portends worse survival.





Are they talking to each other?

- Serum creatinine is one of three variables that form the model of end-stage liver disease (MELD) score currently used in determining priority for orthotopic liver transplantation (OLT) and predict 3-month mortality.

The MELD Model, UNOS Modification

In the following model, survival probability of a patient with end-stage liver disease is estimated based on the following variables. Please enter data in the corresponding boxes.

What is the INR?	
What is the bilirubin?	(mg/dl)
What is the creatinine?	(mg/dl)
Has the patient had dialysis at least twice in the past week?	○ No ○ Yes

Compute

MELD score:

Reset

MELD = 3.78 x $\log_e$ serum bilirubin (mg/dL) +

11.20 x $\log_e$ INR +

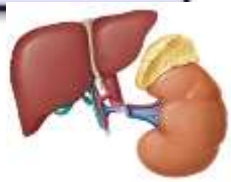
9.57 x $\log_e$ serum creatinine (mg/dL) +

6.43 (constant for liver disease etiology)

NOTES:

If the patient has been dialyzed twice within the last 7 days, then the value for serum creatinine used should be 4.0

Any value less than one is given a value of 1 (i.e. if bilirubin is 0.8, a value of 1.0 is used) to prevent the occurrence of scores below 0 (the natural logarithm of 1 is 0, and any value below 1 would yield a negative result)



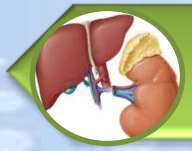
Treatment

MELD SCORE

The Model for End-Stage Liver Disease (MELD)

In interpreting the MELD Score in hospitalized patients, the 3 months mortality is:

- 40 or more — 71.3% mortality
- 30–39 — 52.6% mortality
- 20–29 — 19.6% mortality
- 10–19 — 6% mortality
- <9 — 1.9% mortality



Are they talking to each other?

- Pre transplantation creatinine was found to be the most powerful predictor of survival post-OLT.

- Patients who are transplanted after developing HRS have significantly decreased survival, increased requirement for early postoperative intermittent or continuous RRT and increased risk of other posttransplant complications.

- There may also be incomplete recovery of renal function in some HRS patients following liver transplantation with greater risk of progression to end-stage renal disease.

Weismuller TJ (2008)

Kidney dysfunction in cirrhotic patients

Acute

Chronic

HRS 2

Glomerulonephritis (HCV, HBV related)

Immunoglobulin A nephropathy

Diabetic nephropathy

AKI in Cirrhotic patients

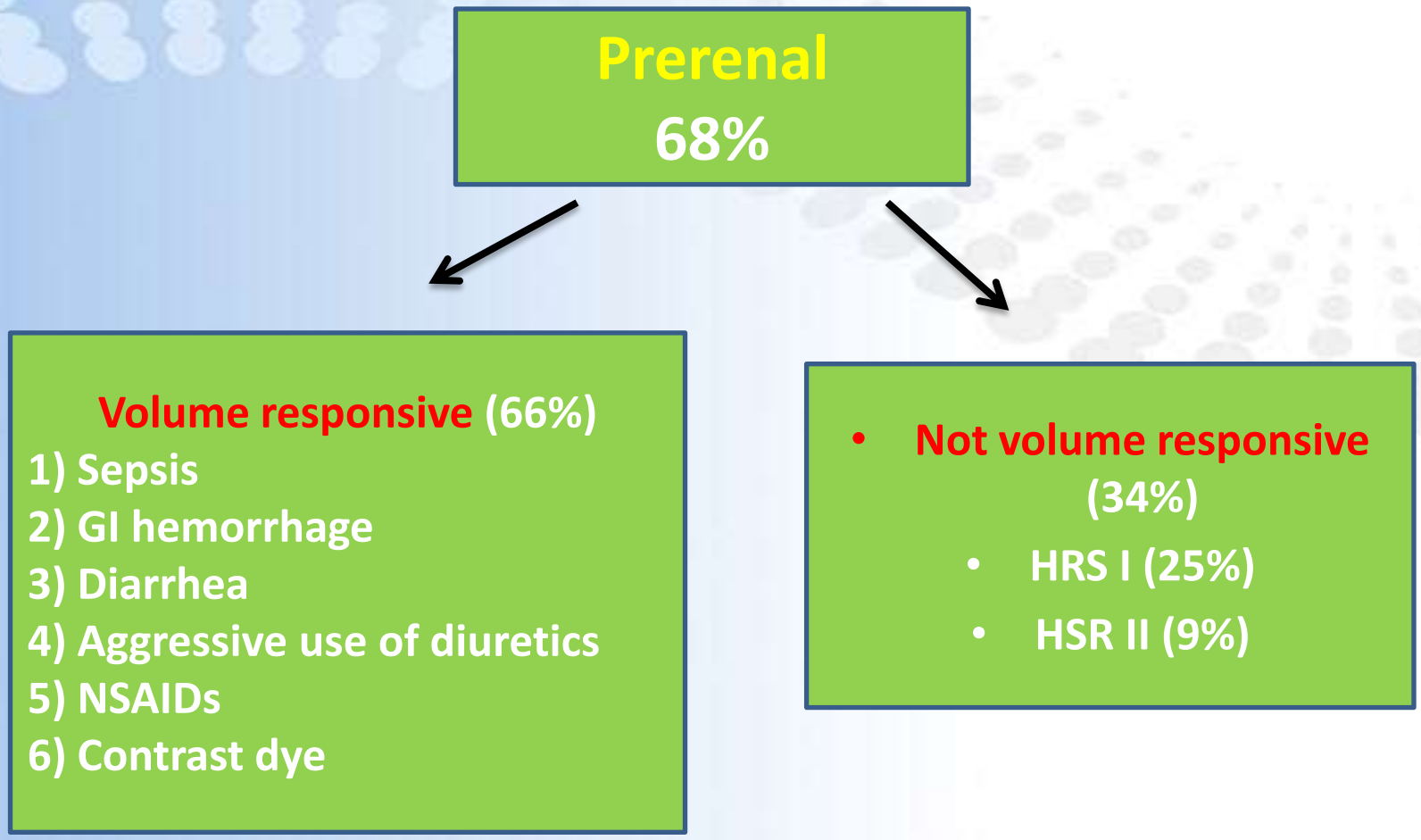
- **Prerenal** 68%
- **Intrarenal** 32%
- **Post renal** < 1%

Prevalence of AKI in cirrhotic patients in different clinical settings

Clinical setting	Prevalence
Hospitalized cirrhotic patients	20% present with AKI at admission 70% present with AKI during hospitalization 17% present with AKI on top of CKD during hospitalization
On admission for liver transplantation	25% present with loss 16% present with failure
Post operative after liver transplantation	12-70% present with AKI 71% of patients who present with AKI require RRT
Patients admitted in ICU (RIFLE)	49% present with some degree of AKI during ICU stay 22% develop risk during ICU stay 19% develop failure during ICU stay
Patients with SBP	40.8-55.9% have AKI
TIPS related AKI	5.5-5.8% develop AKI after TIPS

Muciono J et al. 2012, ANNALS of Hepatology

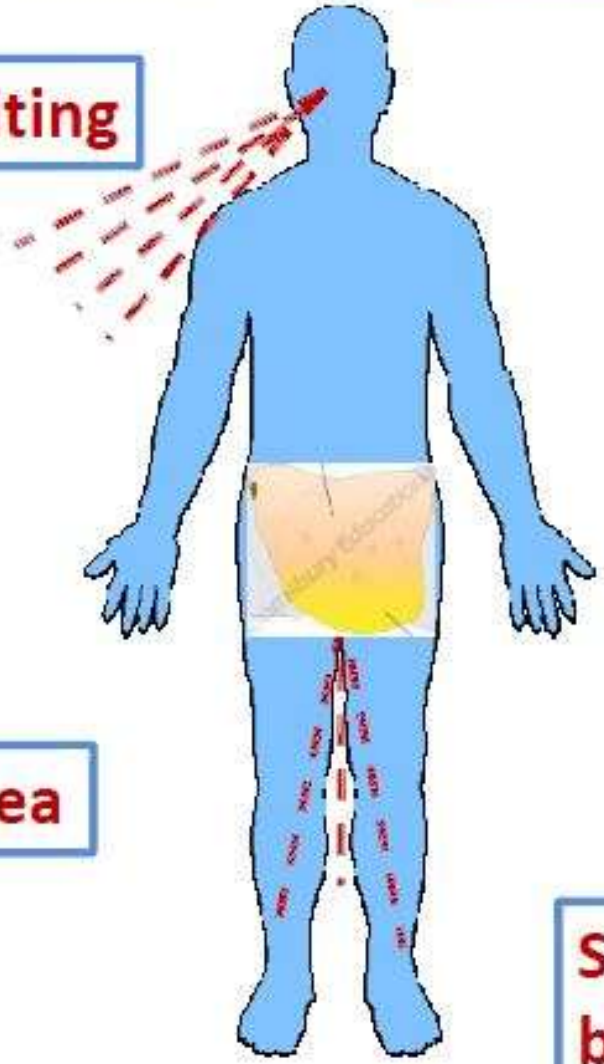
Prerenal failure


Prerenal
68%
Volume responsive (66%)
1) Sepsis
2) GI hemorrhage
3) Diarrhea
4) Aggressive use of diuretics
5) NSAIDs
6) Contrast dye
Not volume responsive (34%)
HRS I (25%)
HSR II (9%)

Detailed history:

Reduced sodium intake

Vomiting



GIT bleeding

Diarrhea

Spontaneous bacterial peritonitis

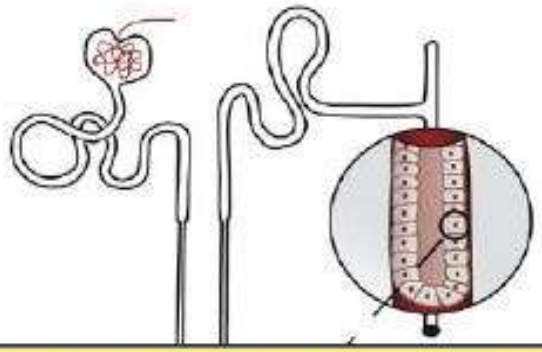
Lactulose therapy

Intensive diuretic therapy

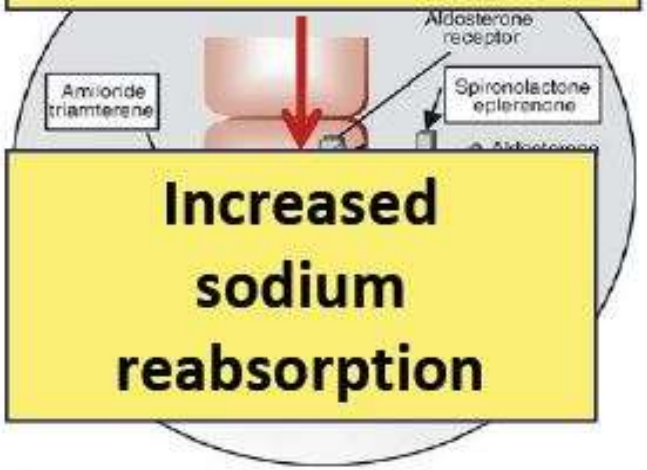
Abuse of NSAIDS

Paracentesis without replacement

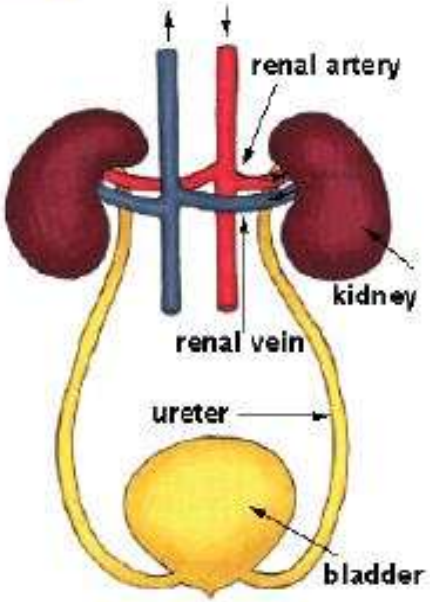
Lab investigations:



Intact tubular cells function



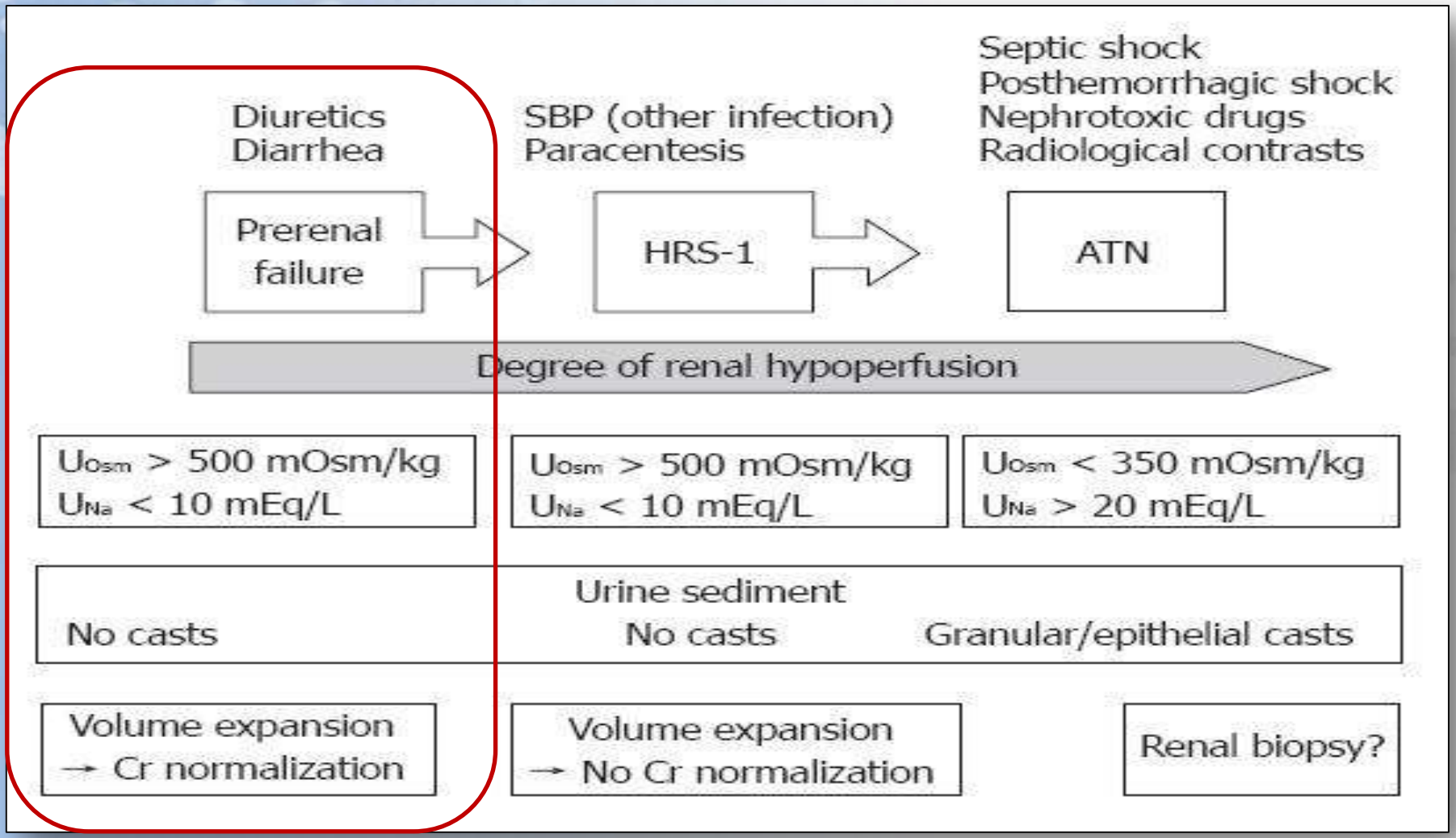
Increased sodium reabsorption



Urine concentration

Urine Na

Diagnosis



Differential diagnosis of three forms of acute kidney injury in patients with decompensated cirrhosis.

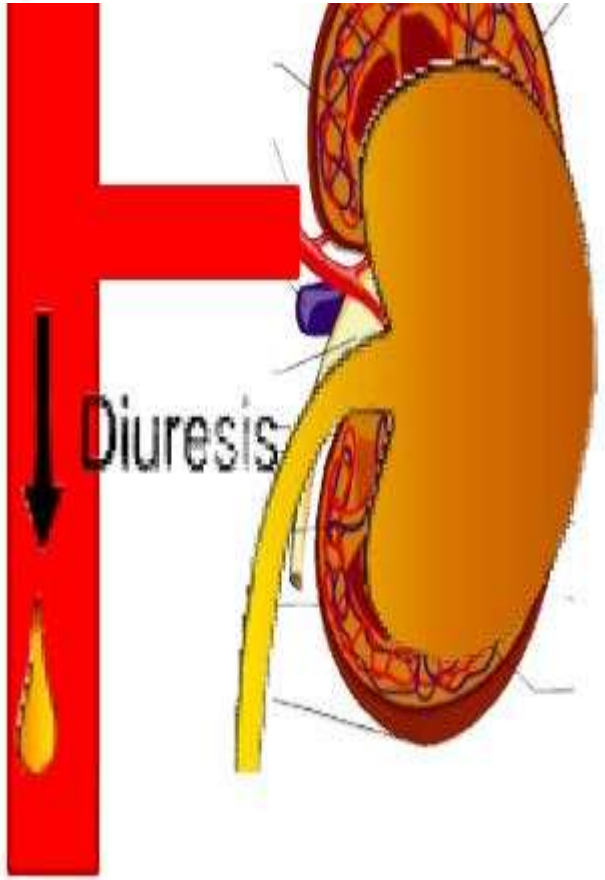
Response to volume expander

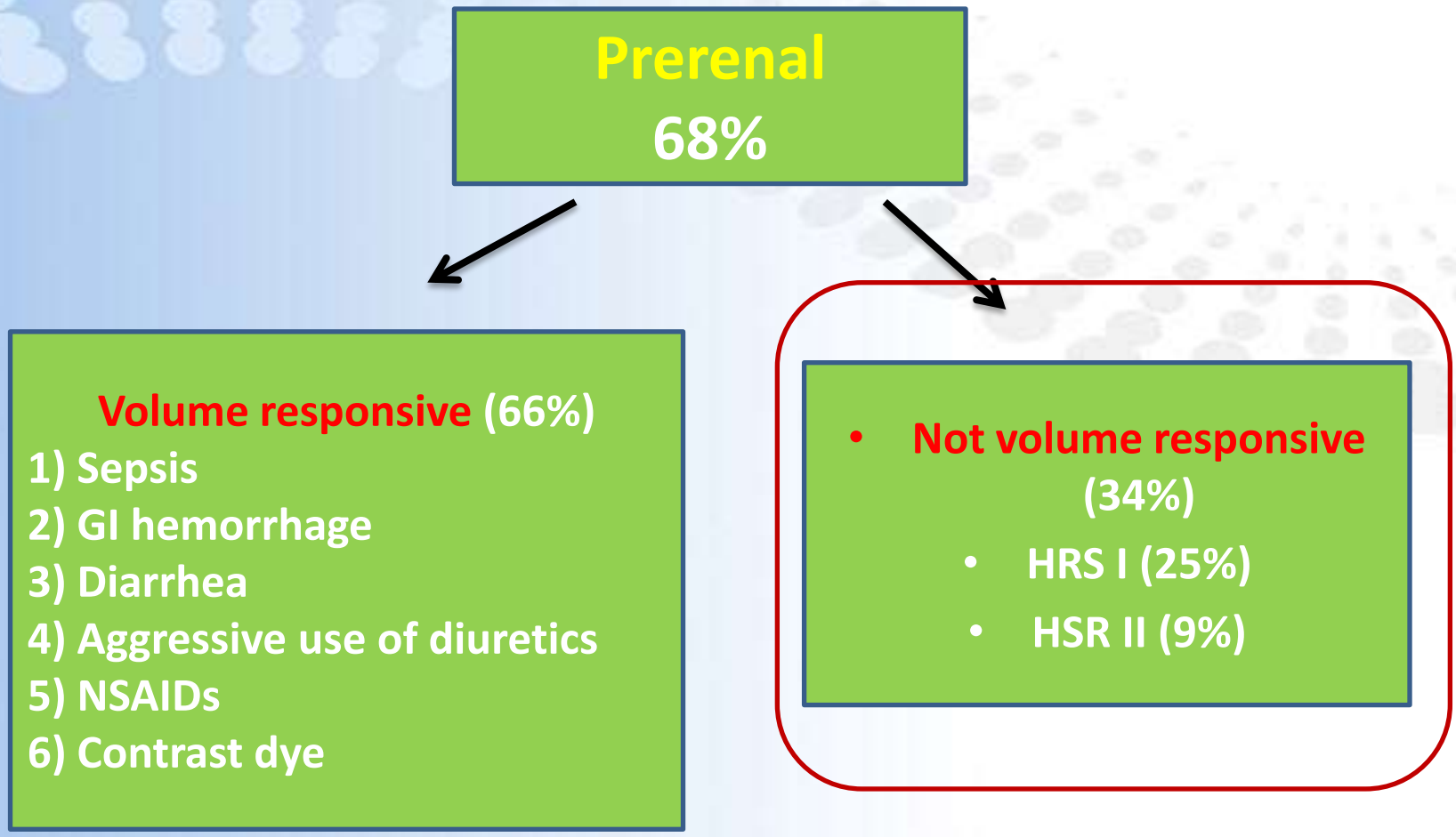
↓

Restoration of effective circulatory volume and renal perfusion

↓

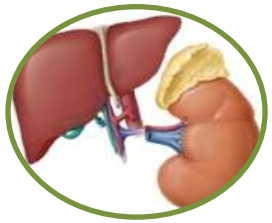
Improving condition




Prerenal
68%
Volume responsive (66%)
1) Sepsis
2) GI hemorrhage
3) Diarrhea
4) Aggressive use of diuretics
5) NSAIDs
6) Contrast dye
• Not volume responsive (34%)
• HRS I (25%)
• HSR II (9%)

Hepatorenal syndrome (HRS)

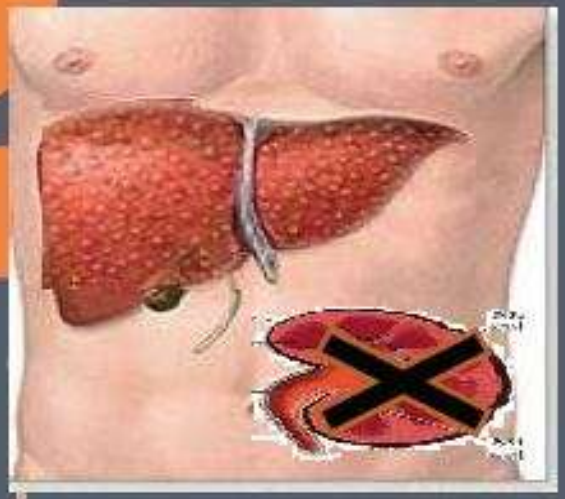
Hepatorenal syndrome



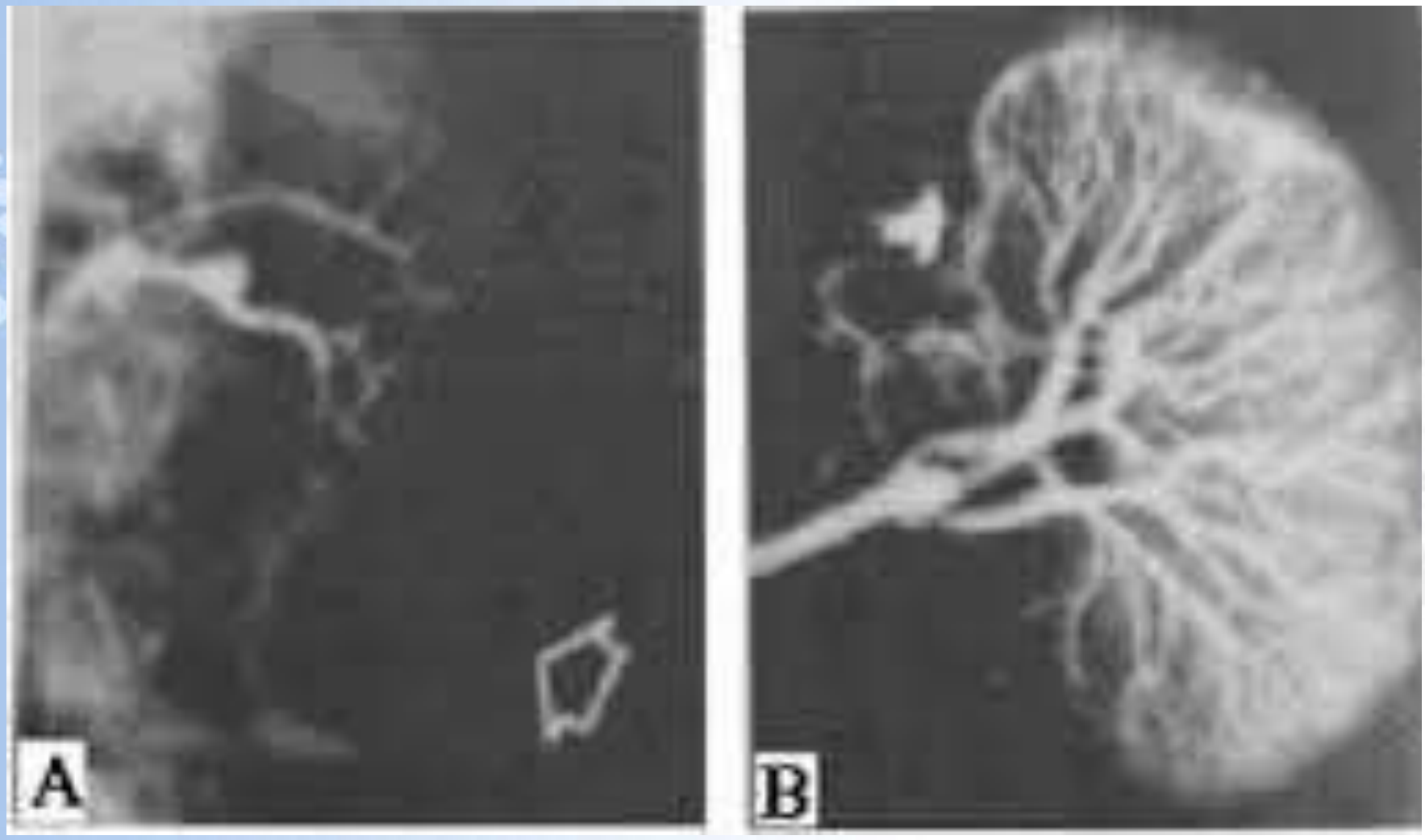
- Hepatorenal syndrome (HRS) is a potentially reversible , functional renal failure that occurs in patients with acute or chronic liver disease, with advanced failure and portal hypertension.
- HRS characterized with pronounced renal V.C. that result in low GFR and marked splanchnic arteriolar V.D. result in reduction in systemic vascular resistance and arterial hypotension.

Why is HRS a unique disorder ?

Normal histological appearance of the kidneys



The kidneys often resume normal function following liver transplantation



At autopsy: Renal angiogram showed complete filling of the renal arterial system up to periphery of the cortex indicating the functional nature of the vascular abnormality in HRS.

Incidence of HRS

- The possibility for development of HRS in cirrhotic patients is estimated to be 18% at 1 year and 40% at 5 years.
- The incidence of HRS in acute fulminant liver disease has been reported to be between 20% to 30%.
- 20% of patients with spontaneous bacterial peritonitis (SBP) will develop type 1 HRS, despite rapid resolution of the infection with antibiotics.
- 15% of patients undergoing large-volume paracentesis (> 5L removed) without albumin replacement will also develop type 1 HRS.

Akriviadis E, *Gastroenterology* 2000.

Pseudo HRS

- Pseudohepatorenal syndrome describes concurrent hepatic and renal dysfunction secondary to a wide variety of diseases or exposure to drugs and toxins.
- Both hepatic and renal functional abnormalities are often found at first clinical presentation.
- No evidence of advanced liver failure and portal hypertension.

Pseudohepatorenal syndome

Causes	Tubulointerstitial	Glomerular
Infection	Sepsis, leptospirosis, brucellosis, TB, EB virus, hepatitis A virus	Hepatitis B, C , HIV infection, schistosoma mansoni, liver abscess
Drugs	Tetracycline, rifampicine, sulfonamide, phenytoin allopurinol,methtrexate, acetaminophen overdose	
Toxins	CCl4, trichloroethylene, chloroform, elemental phosphorus, arsenic, copper, chromium, barium, amatoxins,	
Systemic diseases	Sarcoidosis, Sjogren syndrome	SLE, vasculitis, amyloidosis, cryoglobulinemia
Circulatory failure	Hypovolemic or cardiogeic shock	
Malignancy	Lymphoma, leukemia	
Congenital	Polycystic liver and kidney disease,	
Miscellaneous	Fatty liver of pregnancy,Reye syndrome	Eclampsia, HELLP, Cirrhotic glomerulopathy

New International Ascites Club criteria

- Cirrhosis with ascites.
- Serum creatinine >133 µmol/l (1.5 mg/dl).
- No improvement of serum creatinine (decrease to a level of ≤133 µmol/l) after at least two days of diuretic withdrawal and volume expansion with albumin. (albumin is 1 g/kg body weight per day up to a maximum of 100 g/day)
- Absence of shock.
- No current or recent treatment with nephrotoxic drugs.
- Absence of parenchymal kidney disease as indicated by proteinuria >500 mg/ day, microhematuria (>50 red blood cells per HPF) and/or abnormal renal ultrasonography.

Salerno F, Gut 2007.

Pathogenesis of hepatorenal syndrome

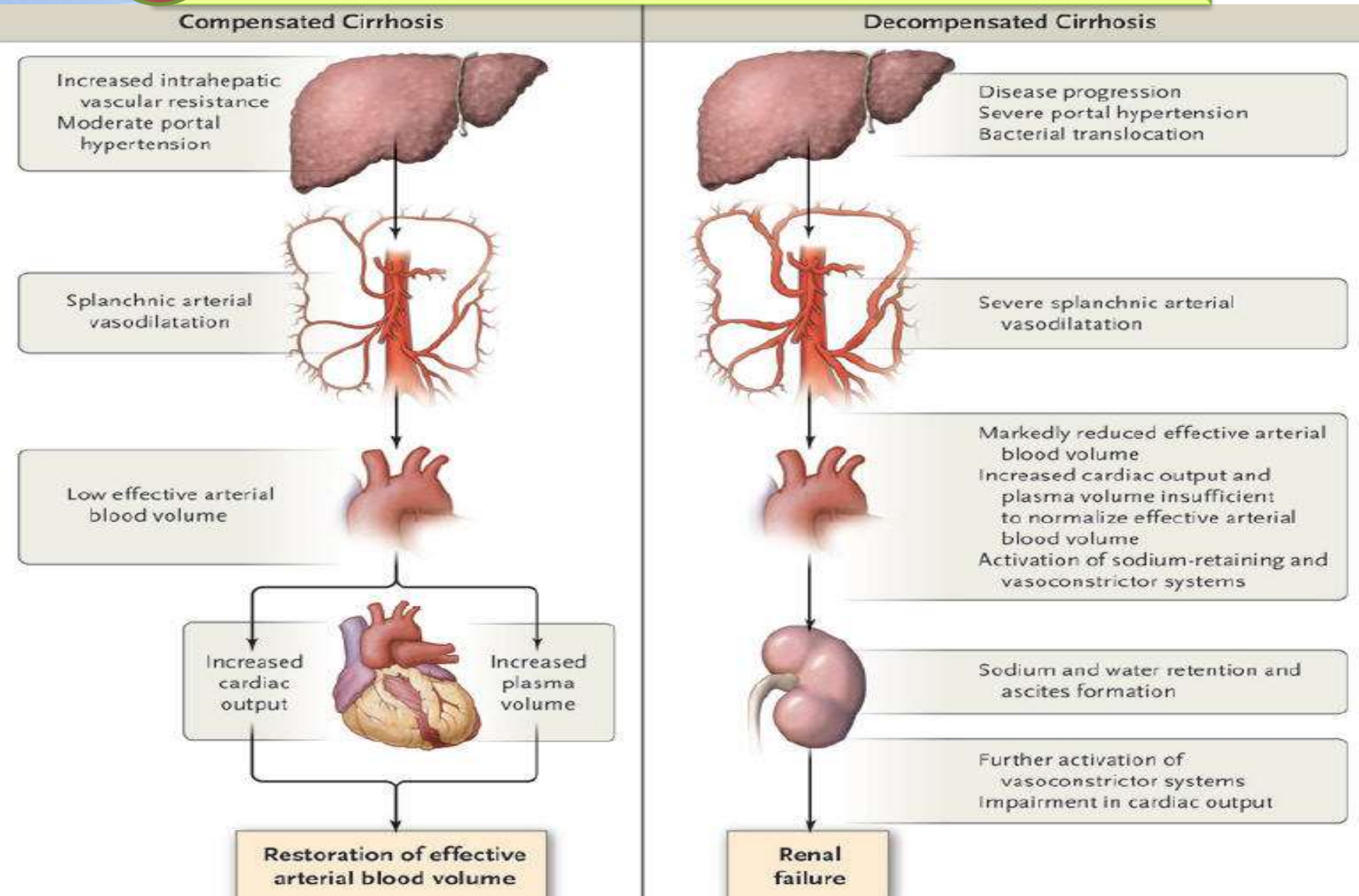
Pathogenesis of hepatorenal syndrome

Renal perfusion depend on systemic and local factors such as:

- COP, systemic MAP
- Basal muscular tone of renal arterioles, renal vascular autoregulation
- Intra-abdominal pressure.

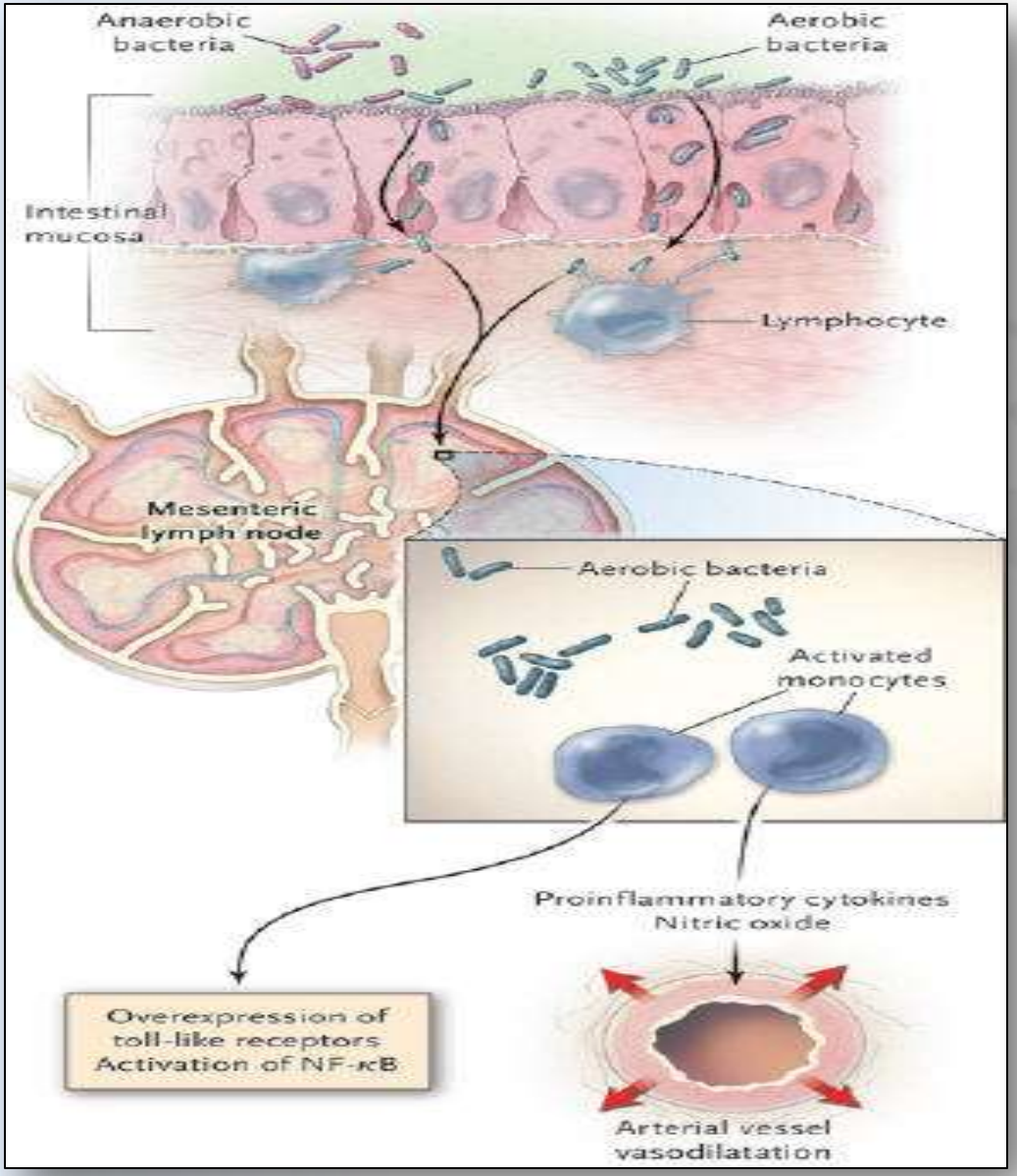
All these factors are affected by end-stage liver cirrhosis

Pathogenesis of hepatorenal syndrome



Pathogenesis of hepatorenal syndrome

Potential Role of Bacterial Translocation and Cytokine Overproduction on Splanchnic Arterial Vasodilatation.



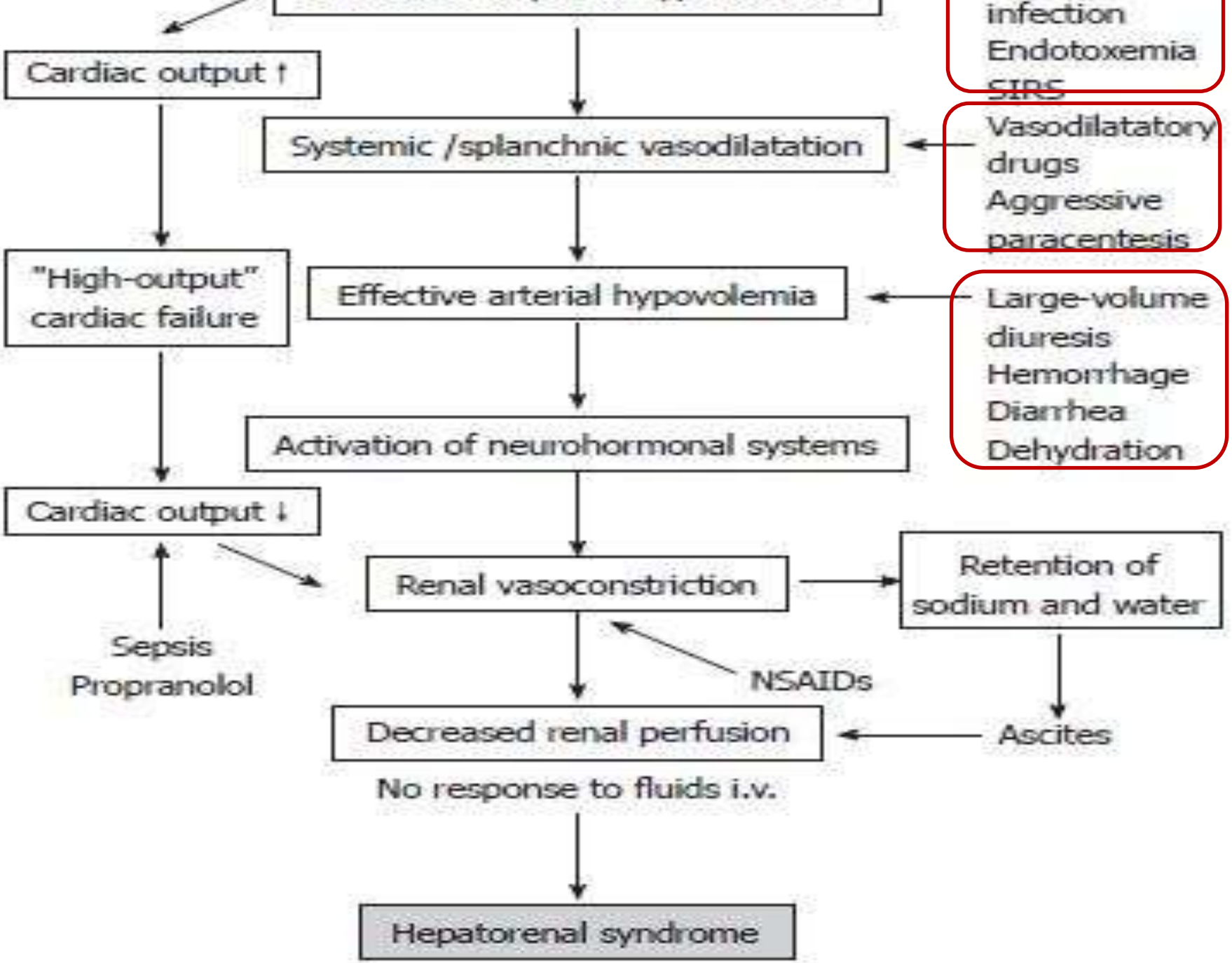
Renal VC *stimulates* the renal vasodilatory Systems (as PGs)

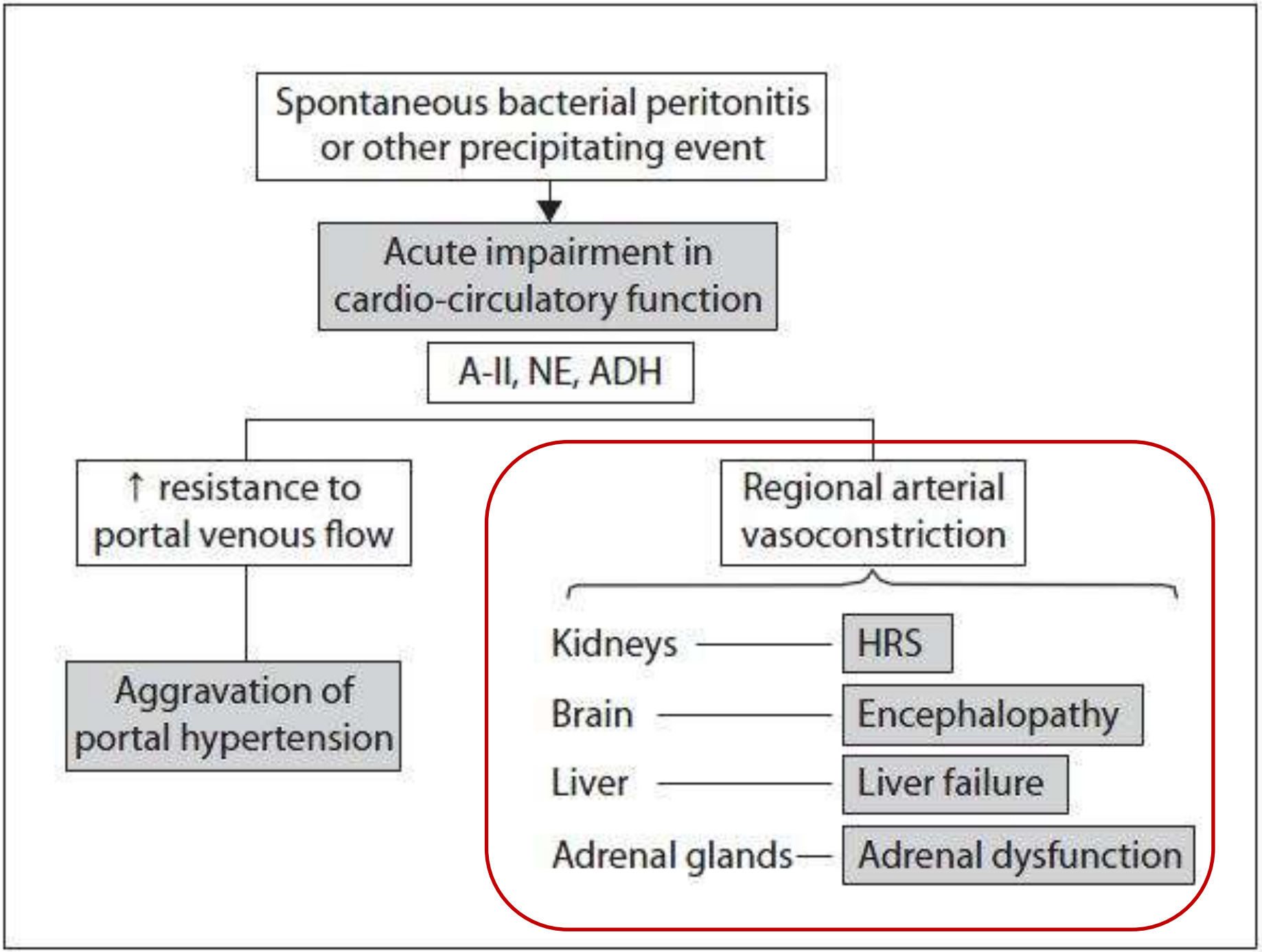
In early phases of cirrhosis, renal Vasodilatory systems *antagonises* the renal effects of the vasoconstricor systems

In advanced cirrhosis, renal vasodilatory systems is *unable to counter balance* the renal effects of the vasoconstricor systems

Pathogenesis of hepatorenal syndrome

- Tense ascites (Intra-abdominal pressure > 20 mmHg) giving rise to abdominal compartment syndrome and severe impairment of renal venous blood flow and secondary disturbances in arterial perfusion of the kidneys.


infection
Endotoxemia
SIRS
Cardiac output ↑
Systemic /splanchnic vasodilatation
Vasodilatatory drugs
Aggressive paracentesis
"High-output" cardiac failure
Effective arterial hypovolemia
Large-volume diuresis
Hemorrhage
Diarrhea
Dehydration
Activation of neurohormonal systems
Cardiac output ↓
Renal vasoconstriction
Retention of sodium and water
Sepsis
Propranolol
NSAIDs
Decreased renal perfusion
Ascites
No response to fluids i.v.
Hepatorenal syndrome


Spontaneous bacterial peritonitis or other precipitating event
Acute impairment in cardio-circulatory function
A-II, NE, ADH
↑ resistance to portal venous flow
Aggravation of portal hypertension
Regional arterial vasoconstriction
Kidneys
HRS
Brain
Encephalopathy
Liver
Liver failure
Adrenal glands
Adrenal dysfunction

Types of hepatorenal syndrome

Type 1 HRS

- Rapid decline in renal function (The serum creatinine doubles to greater than 2.5 mg/dL within 2 weeks).
- HRS 1 constitutes approximately **25%** of the cases of prerenal AKI and **17%** of cases of AKI in hospitalized patients with cirrhosis.
- The annual risk of type 1 HRS development in patients with decompensated cirrhosis is about **20%**, and within 5 years, it increases to **40%**.
- High mortality, with a median survival of only 1 to 2 weeks.
- It can be precipitated by SBP , variceal hemorrhage or total paracentesis without albumin replacement.

Munoz S. Medical Clinics of North America July 2008

Types of hepatorenal syndrome

Type 2 HRS

- Insidous onset and slowly progressive deterioration of renal function (Sr cr increases gradually during several weeks or months) and frequently associated with refractory ascites.
- The median survival of type 2 HRS is about 6 months.
- Many patients with type 2 HRS eventually progress to type 1 HRS because of a precipitating factor.

Munoz S. Medical Clinics of North America July 2008

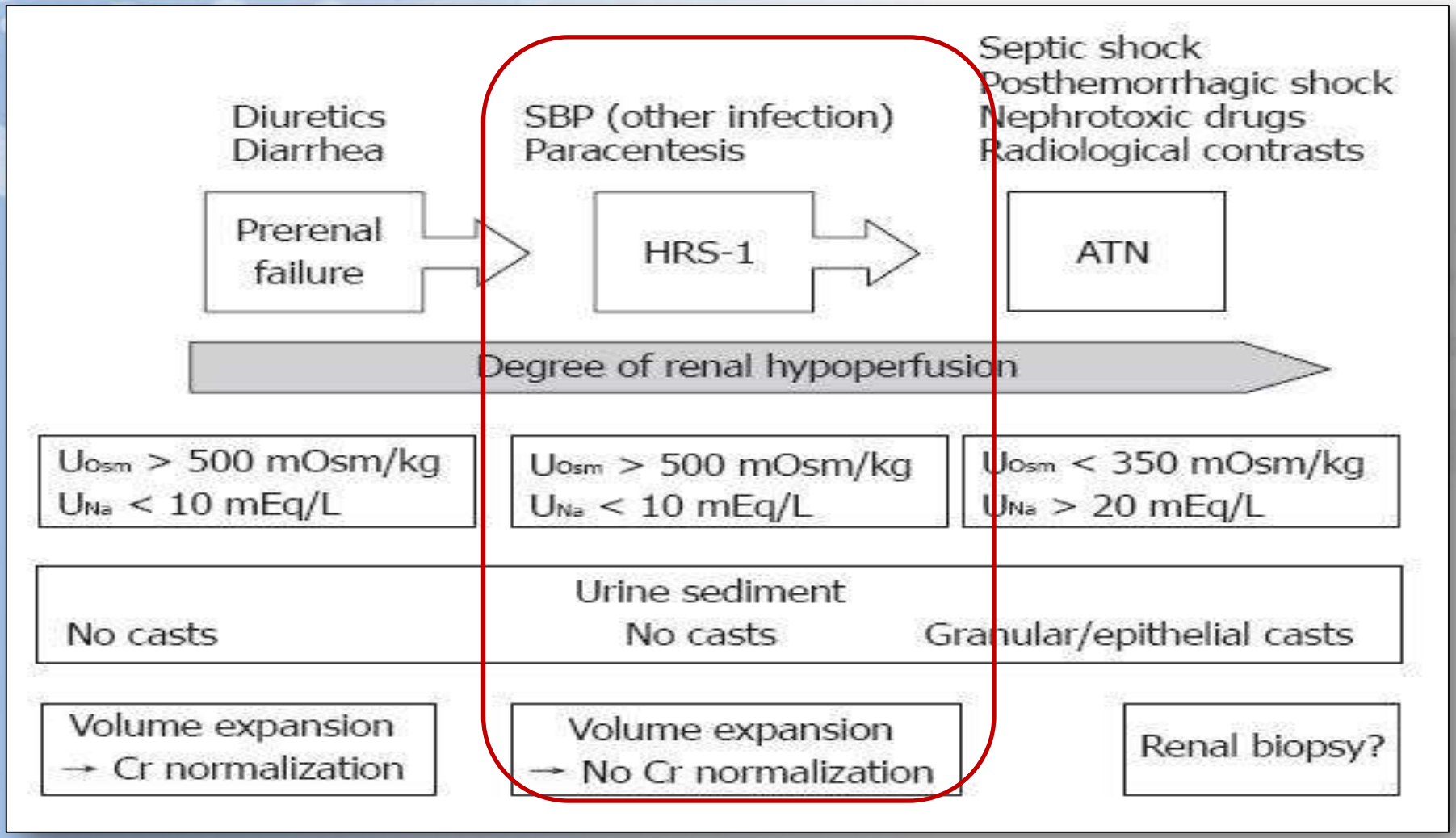
Types of hepatorenal syndrome

- **Type 3 HRS:** (coexistent kidney disease and hepatorenal syndrome)
- Patients with pre-existing renal disease do not meet the traditional diagnostic criteria for HRS.
- A cirrhotic patient with long-standing diabetic nephropathy, obstructive renal disease, or chronic glomerulonephritis can develop HRS from a precipitating event or worsening liver failure.

- **Type 4 HRS (chronic):** (acute liver failure and hepatorenal syndrome)
- HRS complicating ALF, especially when acetaminophen-related.

Munoz S. Medical Clinics of North America July 2008

Diagnosis



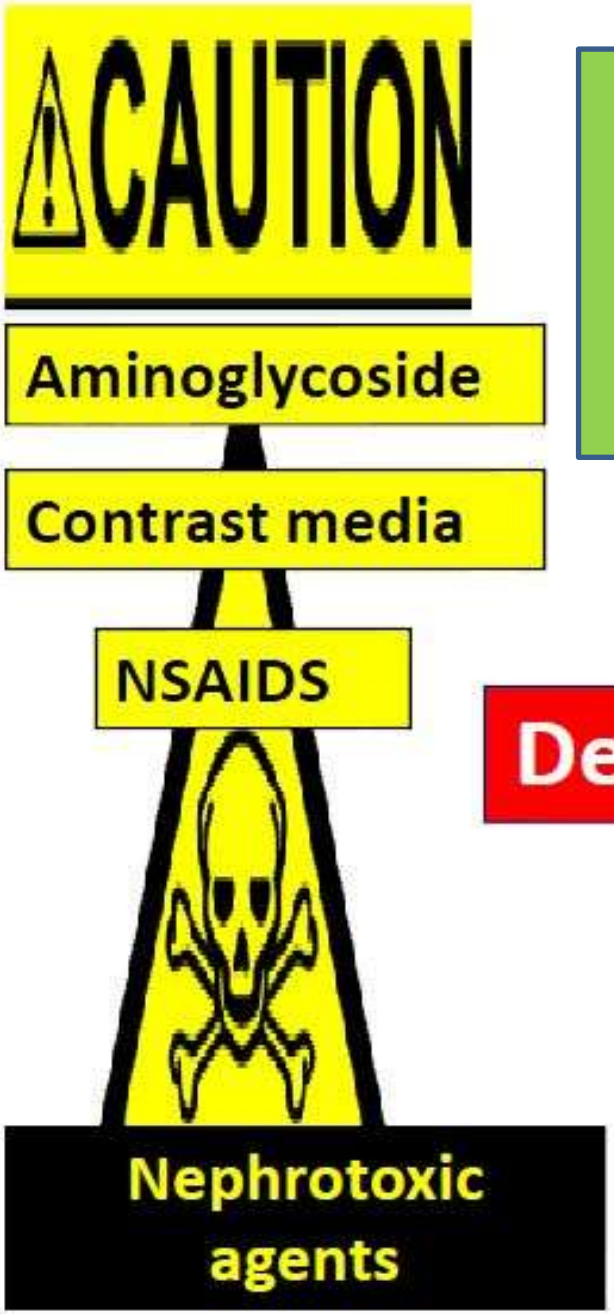
Differential diagnosis of three forms of acute kidney injury in patients with decompensated cirrhosis.

Intrarenal failure

Intrinsic kidney involvement in liver diseases

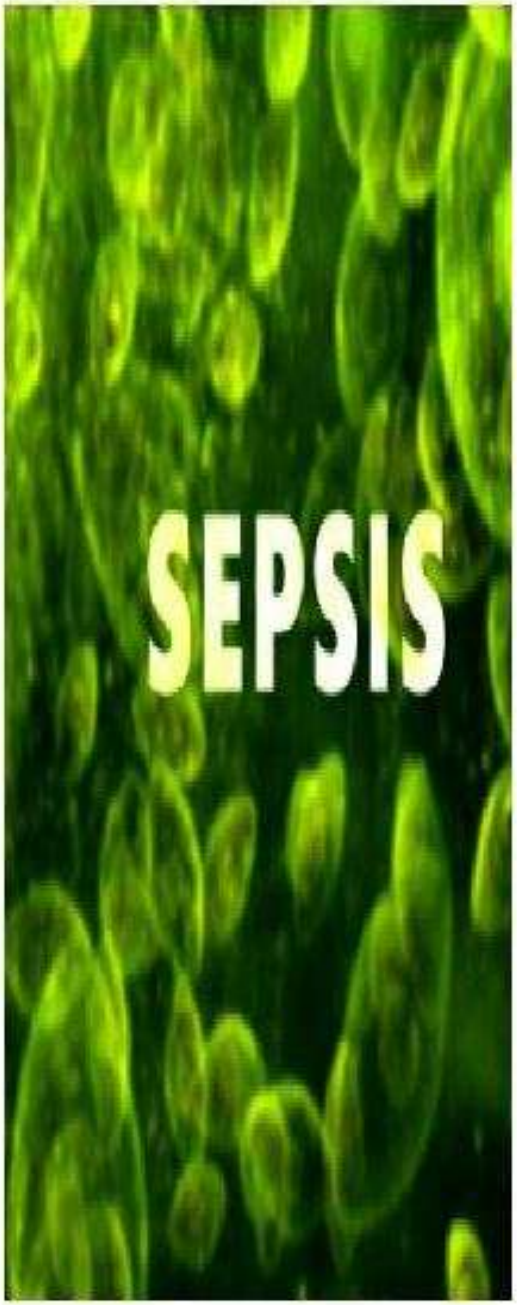
- Tubulo-interstitial involvement
  - Drugs : Paracetamol, ASA, Immunosuppressive drugs
  - Toxin : Mushrooms, Hemoglobin, Myoglobin, Bilirubin, Contrast agents

- Glomerular involvement
  - Hepatitis B,C
  - Type II mixed cryoglobulinemia
  - IgA nephropathy
  - Acute fatty liver and toxemia of pregnancy

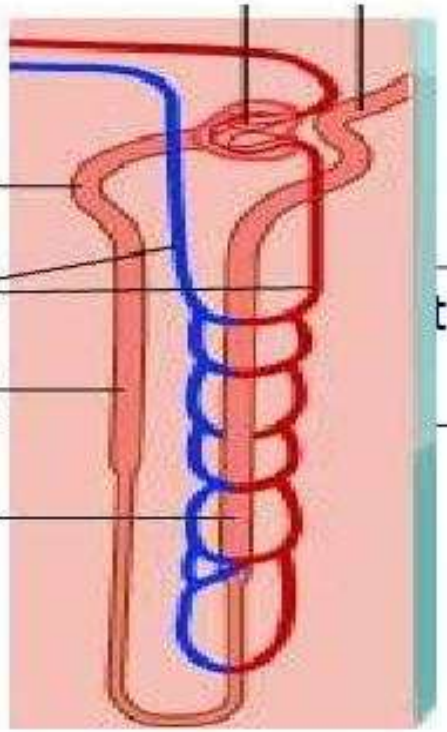


Posthemorrhagic shock,
Prolonged dehydration, severe
Pancreatitis
Major surgical interventions

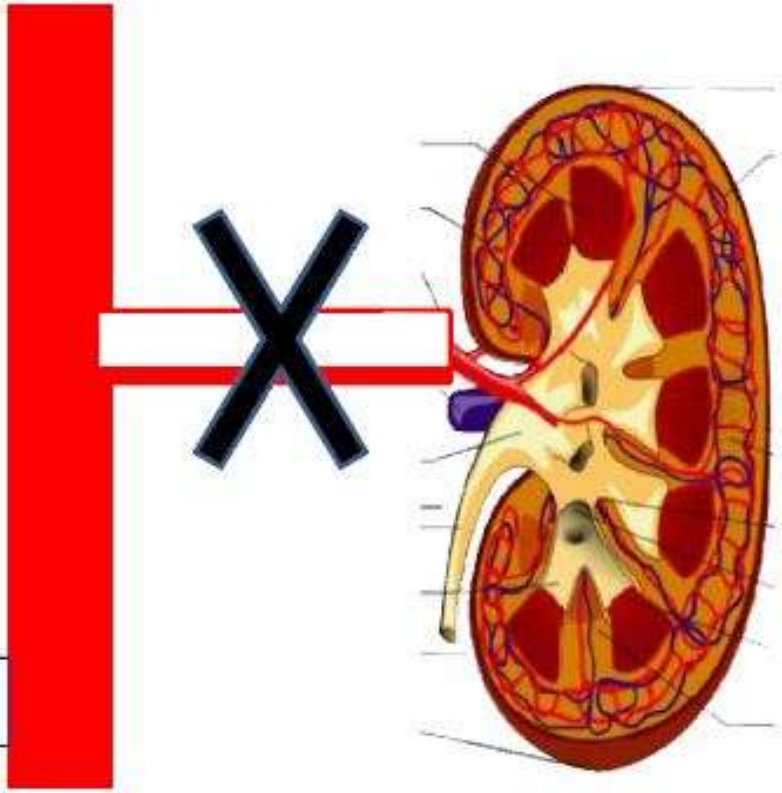
Detailed history:



Urinary abnormality

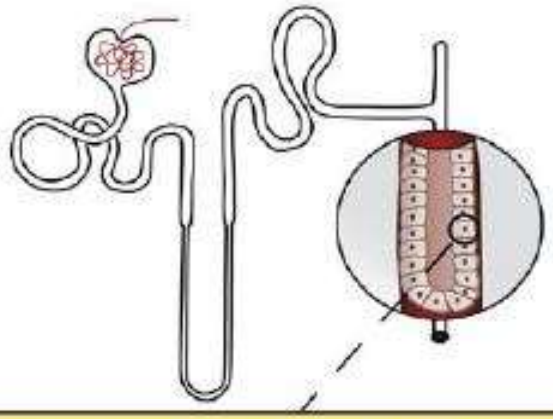


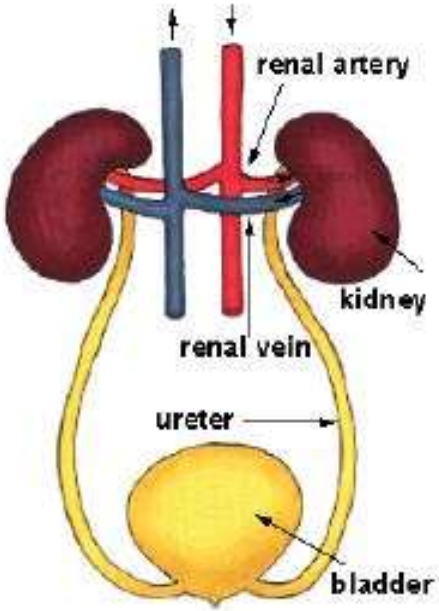
Renal shut down



Altered tubular cells function

Lab investigations:





Disrupted tubular cells function

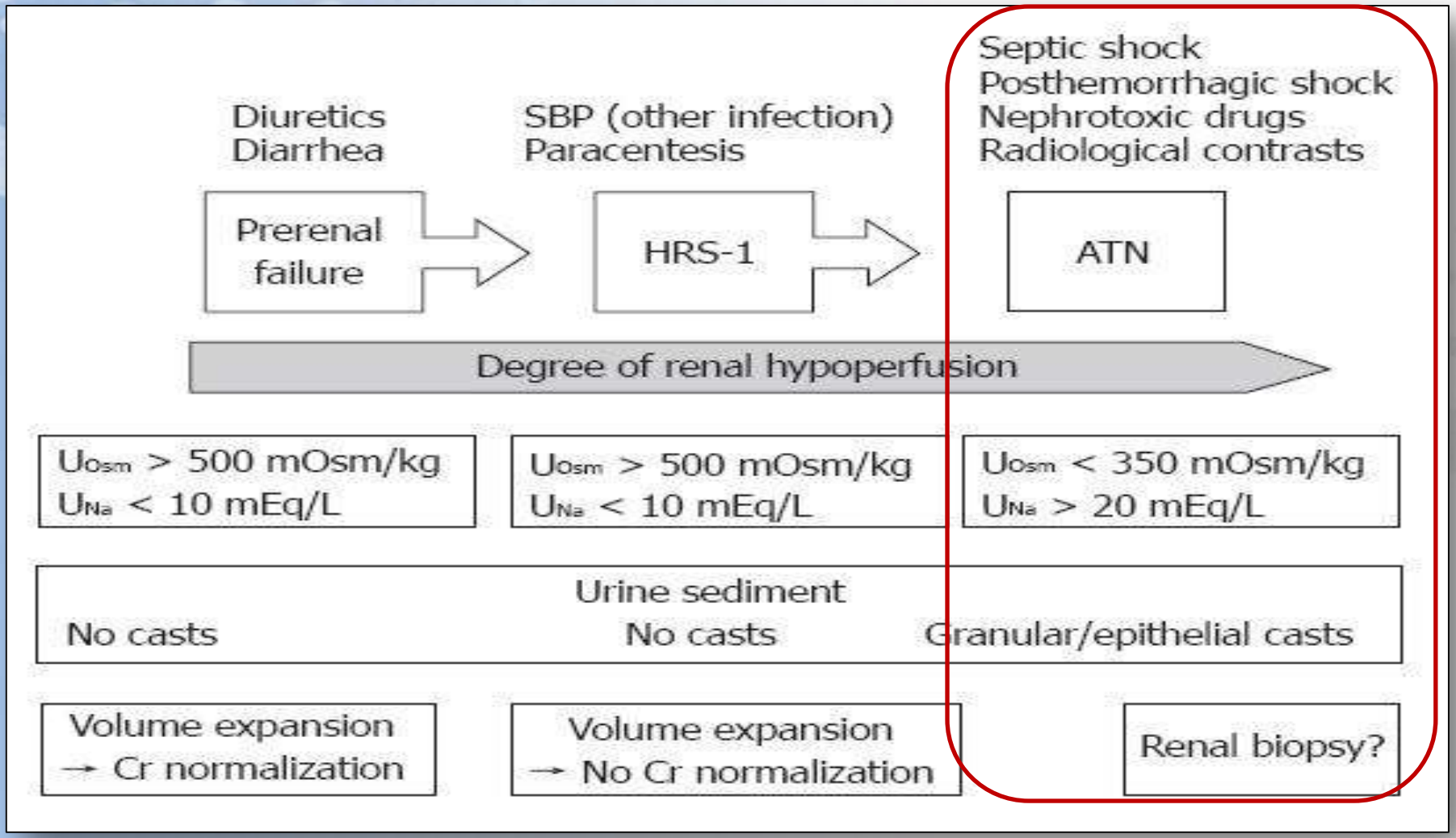
Decreased sodium reabsorption

< 350 mOsm/ kg.

Urine concentration

Urine Na **> 20mEq/L**

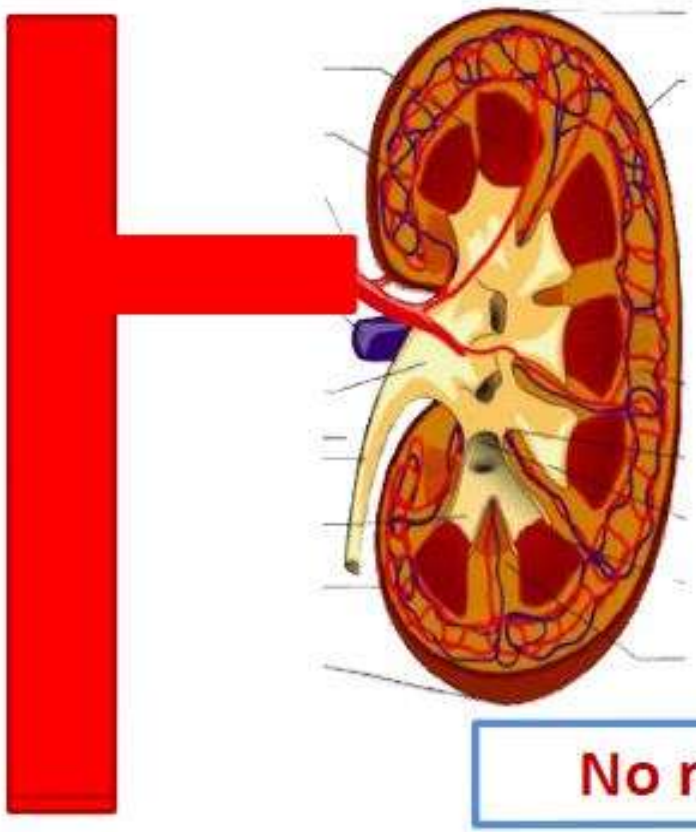
Diagnosis



Differential diagnosis of three forms of acute kidney injury in patients with decompensated cirrhosis.

Response to volume expander

Improving renal perfusion



No response

Interferone renal complicatios

- Interferon therapy for hepatitis C can result in renal complications as interstitial nephritis, proteinuria, mild azotemia and immune complex glomerulonephritis that typically resolve on cessation of therapy.
- The mechanism is obscured. However, immune complex glomerulonephritis due to interferon-anti interferon immune complex that lead to alteration of protein glomerular permeability either directly or through release of other cytokines by activating T lymphocytes

Tovar JL, Int Urol Nephrol. 2008

Postrenal failure

Postrenal failure

- Post renal failure is found in **< 1%** of patients with liver cirrhosis.

Causes

- Nephrolithiasis.
- Benign prostatic hyperplasia
- Kidney tumors, ureter infiltration by tumors of the reproductive organs in women
- Neurogenic urinary bladder.
- Renal papillary necrosis especially alcoholic liver disease patients.

Postrenal failure

- The diagnosis of postrenal failure is based on imaging studies (US and CT) which show urine retention or hydronephrosis.
- The aim of treatment is removal or bypassing the obstruction.

Diagnostic Work Up

Table 2. Acute kidney injury in the patient with liver disease: diagnostic approach[a]

Careful history and physical examination:
Vomiting, diarrhea, gastrointestinal bleeding, marked recent weight loss and rapid decrease in ascites and edema: suspect prerenal azotemia due to gastrointestinal losses or overdiuresis.
Recent exposure to nephrotoxic agents such as nonsteroidal anti-inflammatory agents, aminoglycosides, sulfa-trimethoprim, iodinated radiocontrast, etc: suspect nephrotoxic AKI.
If features of advanced liver disease (especially ascites) are not present, hepatorenal syndrome (HRS) is unlikely.
Urinalysis looking for proteinuria, hematuria, and other sediment abnormalities; random urine protein/creatinine ratio or 24 h urine collection to quantitate proteinuria; urine sodium/osmolality/fractional excretion of sodium.
Differentiating prerenal azotemia from HRS: discontinuation of diuretics and any nephrotoxic medications, and trial of volume expansion with intravenous albumin for at least 48 h.
Rule out abdominal compartment syndrome (if tense ascites are present) by large volume paracentesis + intravenous albumin.
Rule out spontaneous bacterial peritonitis by diagnostic paracentesis for ascitic fluid cell count, gram stain, and culture.
Renal ultrasonography to rule out hydronephrosis/obstructive uropathy.
Monitor blood urea nitrogen, serum creatinine, electrolytes, and liver function tests daily to assess evolution of renal and hepatic status.
Early hepatology and nephrology consultations.

[a]*AKI, acute kidney injury; HRS, hepatorenal syndrome.*

Pitfalls in diagnosis of AKI in hepatic patients

- **Used serum creatinine as parameter of renal function >> delayed diagnosis of AKI**
- Low muscle mass.
- Low protein intake.
- Hyperbilirubinemia or cephalosporins may interfere with the results.
- The edematous state leads to large distribution of Cr in the body
- Complications such as variceal bleeding, SBP or sepsis lead to increased Cr tubular excretion.
- Decreased hepatic production of creatnine.
- **Blood Urea could be low or high**
  - Low protein intake.
  - Lower urea production.
  - GI Bleeding

Management of Acute kidney injury in Liver disease

Advanced liver disease with rise of creatinine and/or decrease urine output

- Discontinue: diuretics, lactulose.
- Investigate and initiate treatment (if present) for infection, blood or fluid losses.
- Albumin IV (1 g/Kg of body weight QD or BID)

Improvement

Continue therapy

No improvement

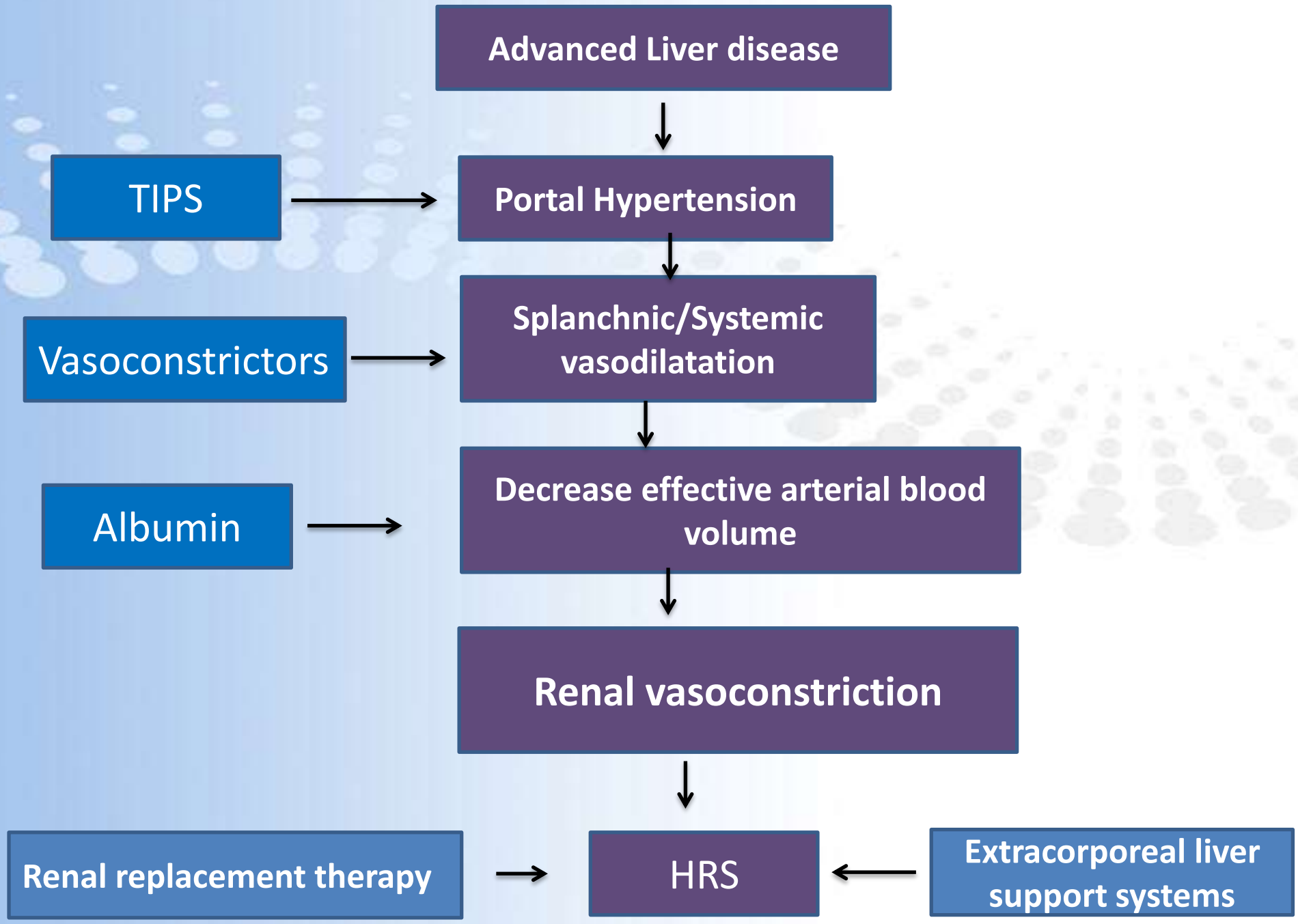
Treat as HRS

Absence of Epithelial cast or CVP> 10

History of shock, nephrotoxin or contrast

Treat as ATN

Epithelial cast or urine markers


Advanced Liver disease
TIPS
Portal Hypertension
Splanchnic/Systemic vasodilatation
Vasoconstrictors
Albumin
Decrease effective arterial blood volume
Renal vasoconstriction
Renal replacement therapy
HRS
Extracorporeal liver support systems

EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER | JOURNAL OF HEPATOLOGY

Clinical Practice Guidelines

Recommendations **Management of type 1 hepatorenal syndrome**

Drug therapy of type 1 hepatorenal syndrome Terlipressin (1 mg/4–6 h intravenous bolus) in combination with albumin should be considered the first line therapeutic agent for type 1 HRS. The aim of therapy is to improve renal function sufficiently to decrease serum creatinine to less than 133 μmol/L (1.5 mg/dl) (complete response). If serum creatinine does not decrease at least 25% after 3 days, the dose of terlipressin should be increased in a stepwise manner up to a maximum of 2 mg/4 h. For patients with partial response (serum creatinine does not decrease <133 μmol/L) or in those patients without reduction of serum creatinine treatment should be discontinued within 14 days (Level A1).

Journal of Hepatology 2010 vol.53 j397–417

Treatment

1- Albumin

- The beneficial effect of albumin in HRS is related to:

a) Plasma volume expansion.

b) Peripheral vasoconstriction due to the ability of albumin to bind NO, endotoxins, bile acids, bilirubin and fatty acids.

Dose: 1 g of albumin/kg on day 1, followed by 40 g/day.

Treatment

2- Vasoconstrictors

A. Terlipressin:

- Vasopressin analogue.

- Dose: 0.5–1 mg every 4–6 hr I.V., with an increase up to 2 mg every 4–6 hr (if SCr does not decrease by 25% on the 3rd day of treatment)
- Usual duration of therapy 5 to 15 days.(lower pretreatment Cr, bilirubin < 10 mg/dl, increased MAP > 5 mm Hg at day 3)

Treatment

2-Terlipressin

- European multicenter, randomized, controlled trial of terlipressin and albumin *vs* albumin monotherapy in 46 patients with both types of HRS demonstrated an improvement in renal function but no survival advantage at 3 mo. Hence, liver transplantation is still the optimal therapy for HRS, and use of terlipressin is considered as a bridge to transplantation.

-Romanelli RG, *World J Gastroenterol* 2006

Treatment

2- Vasoconstrictors

B. Noradrenaline:

- Dose: 0.5–3 mg/hr given as continuous intravenous infusion with the aim of increasing MAP by 10 mm Hg.

Treatment

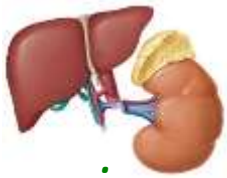
2- Vasoconstrictors

C. Midodrine:

- Selective alpha-1 adrenergic agonist, taken together with octreotide (somatostatin analogue).

- Experimental studies showed that octreotide potentiates the effect of vasoconstrictors. However, octreotide alone is no more effective than placebo and didn't improve SCr.
- These drugs were used in three pilot studies in a total of 79 patients . A complete recovery of renal failure was observed in 49% of patients.

Angeli et al. Journal of Hepatology February 2008

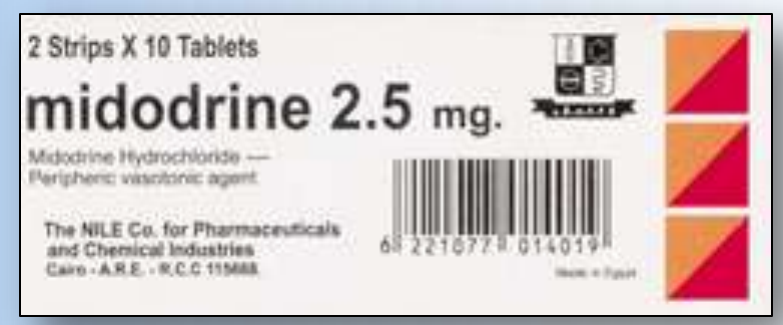


Treatment

2- Vasoconstrictors

C. Midodrine:

- Dose: *Midodrine* 7.5 mg orally 3 times daily, with an increase to 12.5 mg 3 times daily if needed, in association with *octreotide* 100 µg subcutaneously 3 times daily, with an increase to 200 µg 3 times daily if a reduction of serum creatinine was not observed



Treatment

- Treatment can be **stopped**:
- if SCr does not decrease by at least 50% after 7 days at the highest dose.
- In patients with **early response**, treatment should be extended until reversal of HRS (decrease in creatinine below 1.5 mg/dL) or for a maximum of 14 days.
- Vasoconstrictor therapy should be **restarted** if HRS recurs after discontinuation of therapy.
- Once creatinine normalizes, **TIPS** should be considered, particularly if transplantation is not feasible in the near future and the patient has refractory ascites.

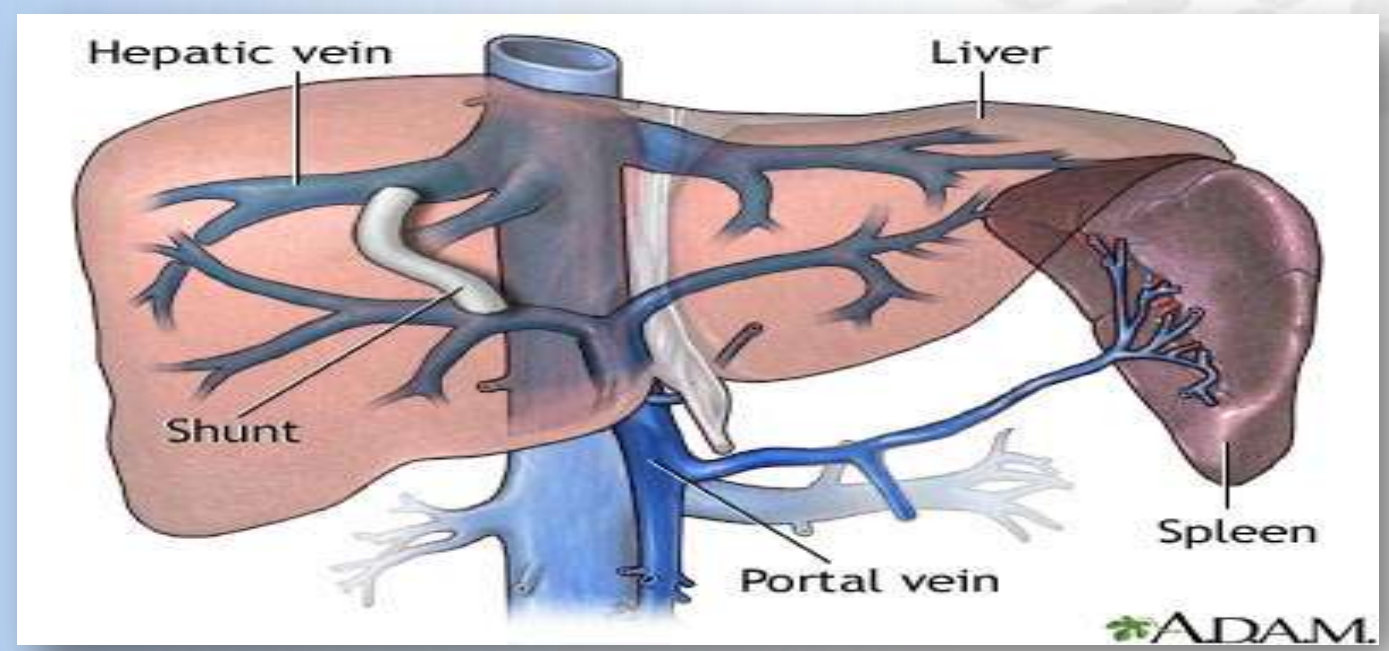
Wong F, et al. HEPATOLOGY 2004

Salerno F, et al. Gut 2007.

Treatment

3- TIPS

- Transjugular intrahepatic portosystemic shunt (TIPS) dramatically lowers the portal pressure .



Treatment

3- TIPS

- The criteria for TIPS insertion are serum bilirubin < 5 mg/dL, INR < 2, and Childs-Pugh score < 12.
- In several studies, significant improvement in SCr and sodium excretion,while renin activity, norepinephrine concentrations decreased gradually after insertion of the TIPS.

Effect of transjugular intrahepatic portosystemic shunt placement on renal function: a 7-year, single-center experie

Abstract

PURPOSE

Transjugular intrahepatic portosystemic shunt (TIPS) creation has been shown to improve renal function in small series of patients with hepatorenal syndrome. The present study examined the effect of TIPS creation on renal function in a large series of patients undergoing TIPS creation who had varying degrees of baseline renal function.

MATERIALS AND METHODS

All de novo TIPS creations during a 7-year period at a single institution were retrospectively reviewed regardless of indication. Pre- and postprocedural laboratory values were obtained and used to calculate Model for End-Stage Liver Disease (MELD) scores and glomerular filtration rates. Subanalysis was performed based on degree of renal insufficiency and indication for the procedure.

RESULTS

A total of 201 successful conventional TIPS procedures were identified. Of those, 72 patients were excluded for lack of follow-up, death during the same hospitalization, lack of TIPS function, or end-stage renal failure requiring dialysis before TIPS creation, leaving 129 procedures. Patients with preprocedural creatinine levels of 1.2-1.9 mg/dL (n = 45) showed an improvement in mean creatinine from 1.5 to 1.1 mg/dL ($P < 10(-12)$) and patients with preprocedure creatinine levels greater than 2.0 mg/dL (n = 21) showed an improvement from 2.8 to 1.5 mg/dL ($P < 10(-5)$). MELD scores decreased in patients with creatinine levels greater than 2.0 mg/dL from 22.1 to 19.2 ($P < 0.005$) but increased in all other patient groups. Amount of iodinated contrast medium administered did not affect creatinine level changes.

CONCLUSIONS

TIPS creation improves renal dysfunction in chronic liver disease. Patients with poorer renal function benefit the most from TIPS creation.

Treatment

3- TIPS

Complications include:

- Portal encephalopathy
- Liver insufficiency.
- Loss of stent function or Bacterial infection of the stent
- Cardiac failure.
- Hemolysis.
- Brensing KA, *Gut* 2000

Treatment

4- Renal replacement therapy

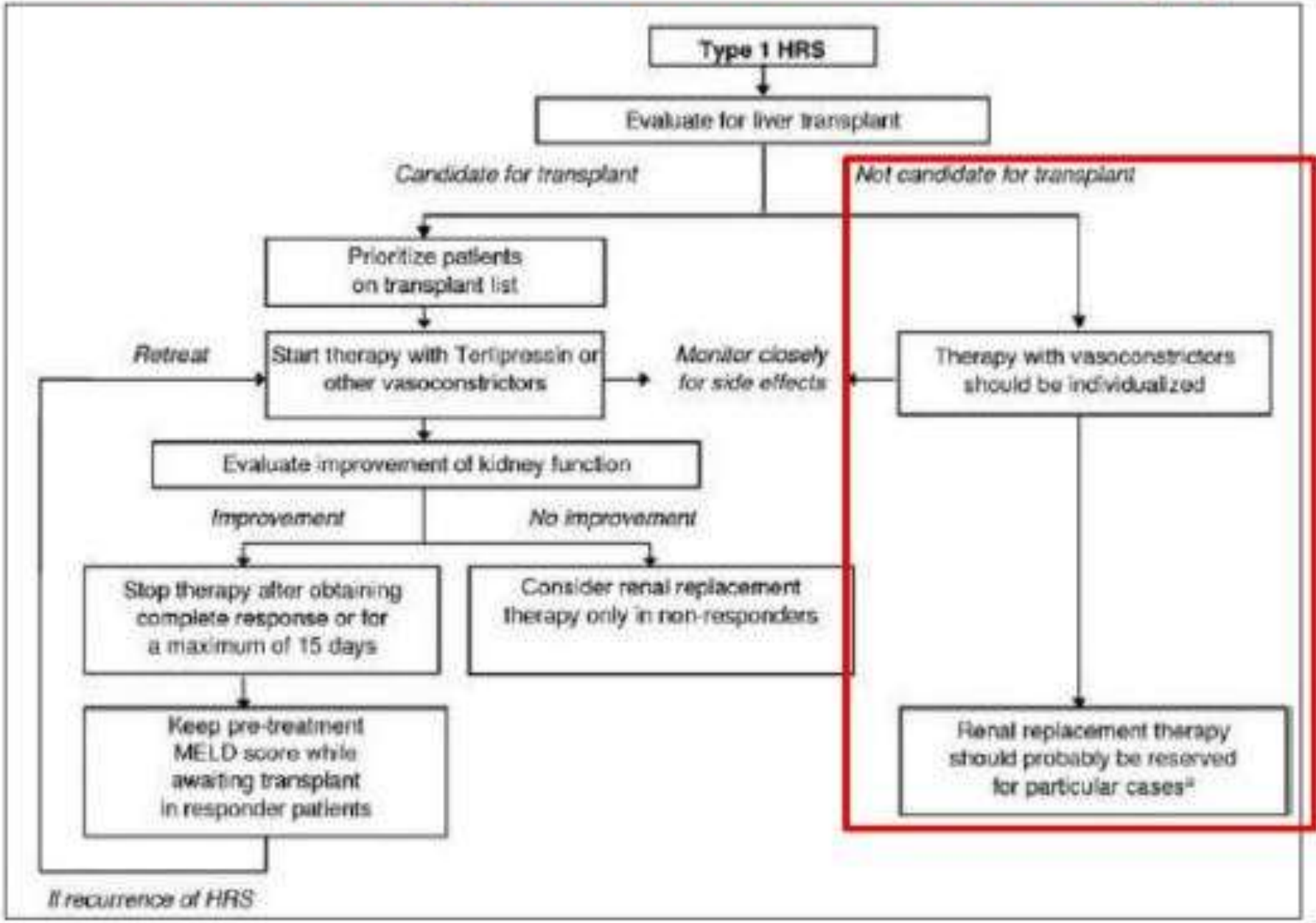
- RRT **should be reserved for:**

1) Patients who are considered orthotopic liver transplantation **(OLT)** candidates in whom pharmacological treatment is ineffective.
2) Patients who are not candidates for OLT but **might recover renal function** (ATN, hypovolemic AKI).

(Volume overload, persistent metabolic acidosis or hyperkalemia)

- **Witzke O**, et al., reported that eight of 30 patients with HRS survived 30 d with use of continuous venovenous hemodialysis in the intensive care unit setting.
- Witzke O, et al., *J Gastroenterol Hepatol* 2004

Renal Replacement Therapy



Treatment

4- Renal replacement therapy

Liver/Kidney replacement therapy:

- Molecular Adsorbent Recirculating System (MARS)
- Single-Pass Albumin Dialysis Extended. (SPAD)
- Prometheus
- These systems are designed to remove albumin bound toxins, (NH_3, bilirubin, creatinine), only achieve a temporary improvement in metabolic abnormalities that result from liver and kidney insufficiencies.

Liver Transpl. 2000 May;6(3):277-86.

Improvement of hepatorenal syndrome with extracorporeal albumin dialysis MARS: results of a prospective, randomized, controlled clinical trial.

Mitzner SR[1], Stange J, Klammt S, Risler T, Erley CM, Bader BD, Berger ED, Lauchart W, Peszynski P, Freytag J, Hickstein H, Loock J, Löhr JM, Liebe S, Emmrich J, Korten G, Schmidt R.

Author information

Abstract

In hepatorenal syndrome (HRS), renal insufficiency is often progressive, and the prognosis is extremely poor under standard medical therapy. The molecular adsorbent recirculating system (MARS) is a modified dialysis method using an albumin-containing dialysate that is recirculated and perfused online through charcoal and anion-exchanger columns. MARS enables the selective removal of albumin-bound substances. A prospective controlled trial was performed to determine the effect of MARS treatment on 30-day survival in patients with type I HRS at high risk (bilirubin level, > or =15 mg/dL) compared with standard treatment. Thirteen patients with cirrhosis with type I HRS were included from 1997 to 1999. All were Child's class C, with Child-Turcotte-Pugh scores of 12.4 +/- 1. 0, United Network for Organ Sharing status 2A, and total bilirubin values of 25.7 +/- 14.0 mg/dL. Eight patients were treated with the MARS method in addition to hemodiafiltration (HDF) and standard medical therapy, and 5 patients were in the control group (HDF and standard medical treatment alone). None of these patients underwent liver transplantation or received a transjugular intrahepatic portosystemic shunt or vasopressin analogues during the observation period. In the MARS group, 5.2 +/- 3.6 treatments (range, 1 to 10 treatments) were performed for 6 to 8 hours daily per patient. A significant decrease in bilirubin and creatinine levels ($P < .01$) and increase in serum sodium level and prothrombin activity ($P < .01$) were observed in the MARS group. Mortality rates were 100% in the control group at day 7 and 62.5% in the MARS group at day 7 and 75% at day 30, respectively ($P < .01$). We conclude that the removal of albumin-bound substances with the MARS method can contribute to the treatment of type I HRS.

Gut. 2010 Mar;59(3):381-6. doi: 10.1136/gut.2008.174615. Epub 2009 Aug 25.

Molecular adsorbent recirculating system is ineffective in the management of type 1 hepatorenal syndrome in patients with cirrhosis with ascites who have failed vasoconstrictor treatment.

Wong F[1], Raina N, Richardson R.

Author information

Abstract

BACKGROUND: The pathogenetic mechanism of hepatorenal syndrome (HRS) is paradoxical renal vasoconstriction consequent upon systemic and splanchnic arterial vasodilatation. Molecular adsorbent recirculating system (MARS) is a specialised form of dialysis that clears albumin-bound substances, including vasodilators, and therefore can potentially reduce systemic vasodilatation in cirrhosis.

OBJECTIVE: To assess the efficacy of MARS in improving systemic and renal haemodynamics in patients with cirrhosis with refractory ascites and type 1 HRS not responding to vasoconstrictor therapy.

METHODS: A pilot study was carried out in an academic teaching hospital. The study group comprised six patients with cirrhosis, refractory ascites and type 1 HRS not responding to vasoconstrictor treatment. All patients received 5 days of 6-8 h of MARS dialysis. The main outcome measures were pre-MARS and post-MARS measurements of glomerular filtration rate, renal blood flow, neurohormones, cytokines and nitric oxide (NO), as well as daily biochemistry, haematology and urinary volume.

RESULTS: There were no significant changes in systemic haemodynamics and GFR following MARS treatments, despite a significant reduction in NO concentrations (111.5+/-18.8 micromol/l pre-MARS, to 65.1+/-8.2 micromol/l post-MARS, p=0.05). There was a transient reduction in serum creatinine ($p<0.05$), Child-Pugh and MELD (Model End-Stage Liver Disease) scores with MARS, but no significant difference was observed in neurohormone and cytokine levels. Four of six patients died following MARS treatments.

CONCLUSIONS: In patients with cirrhosis, refractory ascites and type 1 HRS not responding to vasoconstrictor treatment, MARS is ineffective in improving systemic haemodynamics and renal function despite reduction in NO levels, suggesting that vasodilatation in advanced cirrhosis is not due to excess systemic vasodilators alone. Transient reduction in serum creatinine indicates direct removal by MARS, and may not represent improved renal function.

Treatment

4- Renal replacement therapy

- Patients undergoing treatment with adsorbent recirculating systems can experience **hypotension, hypothermia, bradycardia or blood clotting abnormalities associated with use of anticoagulants.**

Mitzner SR, et al. Liver Transpl 2000; 6: 277-286.

Treatment

5- Liver transplantation

EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER | JOURNAL OF HEPATOLOGY

Clinical Practice Guidelines

Liver transplantation

Liver transplantation is the best treatment for both type 1 and type 2 HRS. HRS should be treated before liver transplantation, since this may improve post-liver transplant outcome (Level A1).

Journal of Hepatology 2010 vol.53 j397–417

EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER | JOURNAL OF HEPATOLOGY

Clinical Practice Guidelines

Patients with HRS who respond to vasopressor therapy should be treated by liver transplantation alone. Patients with HRS who do not respond to vasopressor therapy, and who require renal support should generally be treated by liver transplantation alone, since the majority will achieve a recovery of renal function post-liver transplantation. There is a subgroup of patients who require prolonged renal support (>12 weeks), and it is this group that should be considered for combined liver and kidney transplantation (Level B2).

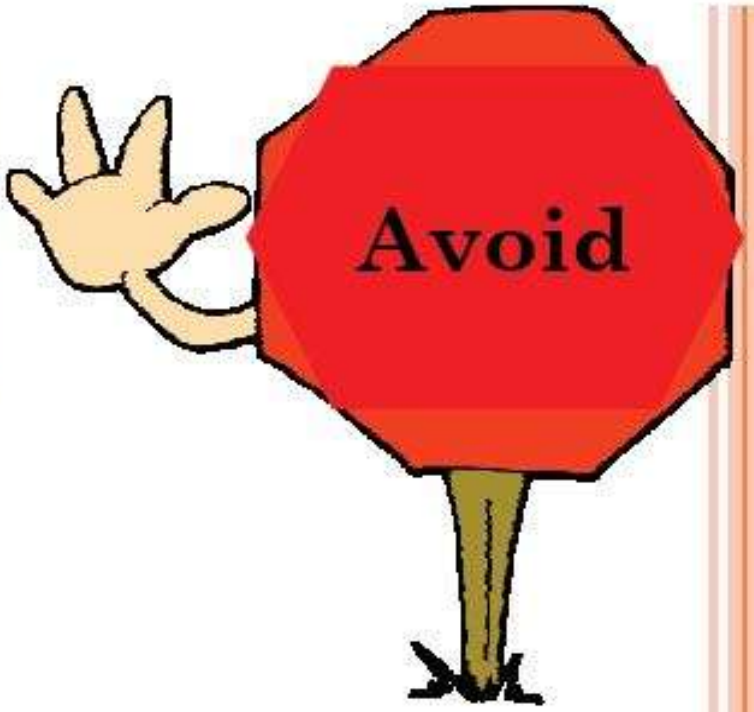
Journal of Hepatology 2010 vol.53 j397–417

- **Prevention of AKI in hepatic patient**

Sepsis

Drugs

NSAIDs
Aminoglycosides
Diuretics



Intravenous albumin

TNF alpha synthesis inhibitor

- In patients with ascites without peripheral edema, the urinary output should not be higher than 1100 mL/d.
- Diuretics should be discontinued if the serum creatinine is > 2.0 mg/dL (180 µmol/d) and serum sodium is < 120 mEq/L, despite fluid restriction, or in the case of encephalopathy.
- Intravenous use of furosemide is not recommended as a dose of 80 mg has been shown to cause an acute reduction in renal blood flow and subsequent azotemia in patients with cirrhosis and ascites.

EASL EUROPEAN ASSOCIATION FOR THE STUDY OF THE LIVER | JOURNAL OF HEPATOLOGY

Clinical Practice Guidelines

Prevention of hepatorenal syndrome

Patients who present with SBP should be treated with intravenous albumin since this has been shown to decrease the incidence of HRS and improve survival (Level A1).

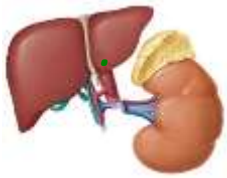
There are some data to suggest that treatment with pentoxifylline decreases the incidence of HRS in patients with severe alcoholic hepatitis and advanced cirrhosis and treatment with norfloxacin decreases the incidence of HRS in advanced cirrhosis, respectively. Further studies are needed (Level B2).

Journal of Hepatology 2010 vol.53 j397–417

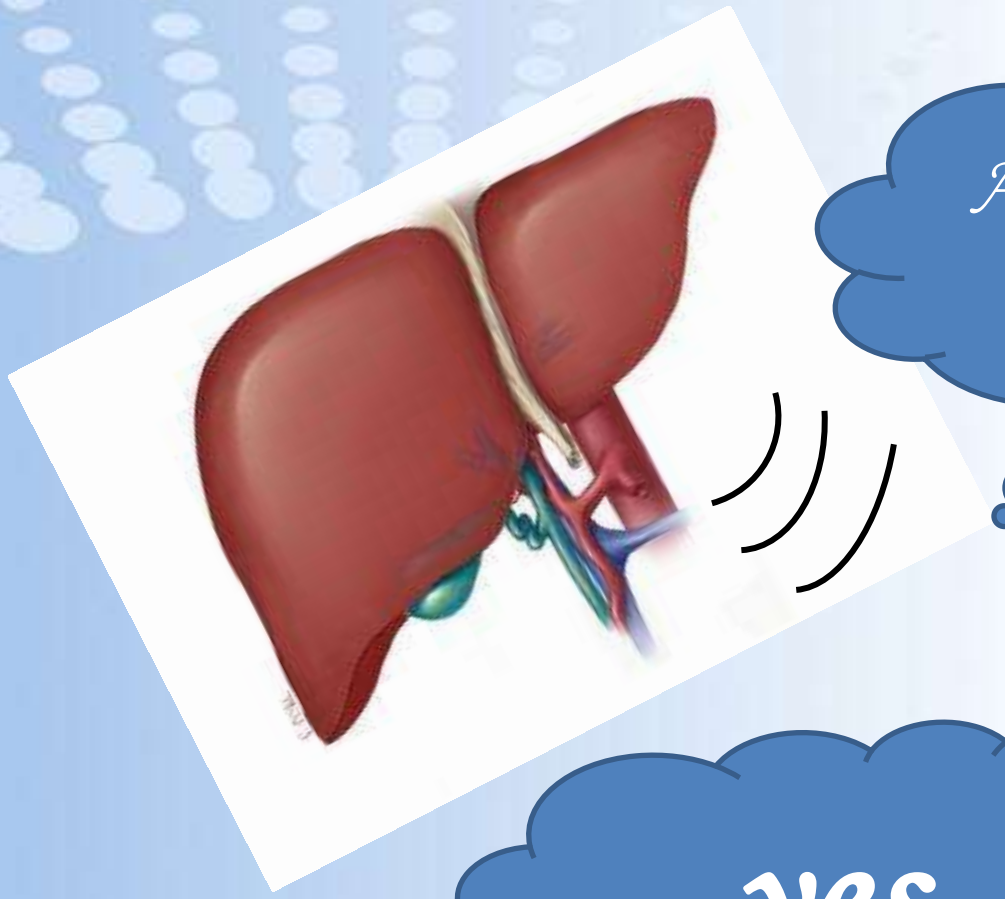
Prevention

Pentoxifylline

- An inhibitor of TNF-α, which plays a major role in the pathogenesis of alcoholic hepatitis and endotoxin-mediated liver injury.
- In a French study, the chronic oral use of pentoxifylline (400 mg, 3 times daily) in patients with advanced cirrhosis of a different etiology did not decrease short- term mortality, however, it reduced the risk of complications (including AKI) at 2 mo and 6 mo.
- **Lebrec D**, *Gastroenterology* 2010

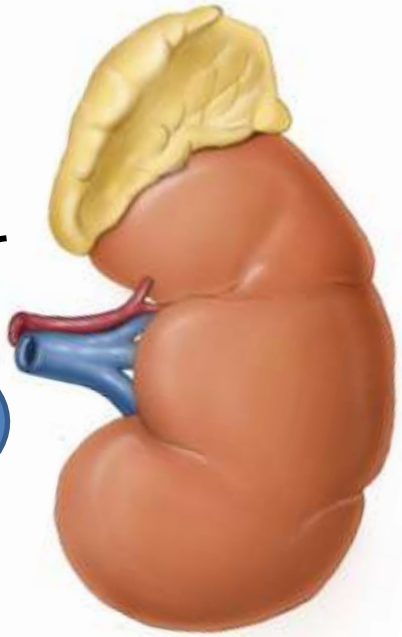


Question ?



Are they talking to each other?

yes




Thank
You